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Physics List

CONTENTS.

	PAGE.
I. Observations upon Cheyne-Stokes' Respiration. By G. NEWTON PITT, M.A., M.D., F.R.C.P., M. S. PEMBREY, M.A., M.D., and R. W. Allen, M.A., M.B.	1
II. Observations upon two Cases of Cheyne-Stokes' Respiration. By FREDERICK TAYLOR, M.D., F.R.C.P., M. S. PEMBREY, M.A., M.D., A. P. BEDDARD, M.A., M.D., F.R.C.P., and HERBERT FRENCH, M.A., M.D., F.R.C.P.	35
III. Aspiration of a Pneumothorax under the X-Rays. By JOHN FAWCETT, M.D.	49
IV. Micrococcus Melitensis and Antiserum. By J. W. H. EYRE, M.D.	55
V. A Note on so-called "Metastatic Pulmonary Cerebral Abscess." By H. C. Cameron, M.B., B.C. ...	69
VI. Observations on a Case of Chyluria occurring in England. By ARTHUR F. HERTZ, M.A., M.D. Oxon., M.R.C.P.	85
VII. Diphtheroid Organisms in the Throats of the Insane. By J. W. EYRE, M.D., F.R.S. Edin., and J. FROUDE FLASHMAN, M.D., B.Sc.	111
VIII. Mechanical Principles in Dentistry. By J. B. PARFITT, L.R.C.P., M.R.C.S., L.D.S. Eng. ...	139
IX. The Relation of the Kidneys to Metabolism. By F. A. BAINBRIDGE, M.A., M.D., and A. P. BEDDARD, M.A., M.D.	149
X. Secretin in Relation to Diabetes Mellitus. By F. A. BAINBRIDGE, M.A., M.D., and A. P. BEDDARD, M.A., M.D.	161

	PAGE.
XI. The Diastatic Ferment in the Tissues in Diabetes Mellitus. By F. A. BAINBRIDGE, M.A., M.D., and A. P. BEDDARD, M.A., M.D., F.R.C.P.	177
XII. Gastrojejunostomy. By R. P. ROWLANDS, M.S. ...	185
XIII. Primary Embolic Chorion-Epithelioma of the Vagina. By HENRY THOMAS HICKS, F.R.C.S. Eng. ...	209
XIV. Upon the Extent to which Widal's Reaction Persists after Recovery from Typhoid Fever. By M. G. LOUISSON, M.B., and HERBERT FRENCH, M.D. ...	227
XV. The Treatment of Caries of the Ribs. By R. P. ROWLANDS, M.S.	245
XVI. New Growths of the Testicle. By G. W. NICHOLSON, M.A., M.D.	249
XVII. The Place and Value of some Methods of Examination of the Urinary Organs. By R. P. ROWLANDS, M.S.	323
XVIII. Certain Features Characteristic of Teleostean Development. By RICHARD ASSHETON, M.A. ...	345
XIX. The Passage of Food along the Human Alimentary Canal. By ARTHUR F. HERTZ, M.A., M.B. Oxon., M.R.C.P.	389
XX. The Subsequent Histories of Patients who have Recovered after Operations for Perforated Gastric or Duodenal Ulcers. By HERBERT FRENCH, M.A., M.D., F.R.C.P.	429
XXI. The Immediate and Later Results of Gastrojejunostomy for Non-Malignant Lesions of the Stomach or Duodenum. By R. P. ROWLANDS, M.S., and HERBERT FRENCH, M.D.	437
XXII. Specimens Recently added to the Pathological Museum. By LAURISTON E. SHAW, M.D., and JOHN FAWCETT, M.D.	451

List of Gentlemen Educated at Guy's Hospital who have passed the Examinations of the several Universities, or obtained other Distinctions, during the year 1906	459
Medallists and Prizemen for 1906	466
The Physical Society, 1906	468
Clinical Appointments held during the year 1906	468
Dental Appointments held during the year 1906	473
Medical and Surgical Staff, 1907	476
Medical School Staff—Lecturers and Demonstrators...	477
The Staff of the Dental School, 1907	480

LIST OF ILLUSTRATIONS.

PLATES.

	TO FACE
Drs. G. NEWTON PITT, M. S. PEMBREY, and R. W. ALLEN. PAGE	
Illustrating their Paper on Observations upon Cheyne-Stokes' Respiration... ..	34
Dr. JOHN FAWCETT.	
Illustrating his Paper on Aspirations of a Pneumothorax under the X-Rays	50, 53
Mr. R. P. ROWLANDS.	
Illustrating his Paper on Gastrojejunostomy	194, 204
Mr. HENRY THOMAS HICKS.	
Illustrating his Paper on Primary Embolic Chorion-Epithelioma of the Vagina... ..	211, 214, 220
Mr. R. P. ROWLANDS.	
Illustrating his Paper on The Treatment of Caries of the Ribs	246
Mr. G. W. NICHOLSON.	
Illustrating his Paper on New Growths of the Testicle	321

WOODCUTS AND DIAGRAMS.

	PAGE
Drs. G. NEWTON PITT, M. S. PEMBREY, and R. W. ALLEN.	
Illustrating their Paper on Observations upon Cheyne-Stokes' Respiration... ..	8, 9, 26, 27, 28
Drs. TAYLOR, M. S. PEMBREY, A. P. BEDDARD, and HERBERT FRENCH.	
Illustrating their Paper on Observations upon two Cases of Cheyne-Stokes' Respiration ...	38, 40, 41

List of Illustrations.

vii.

Dr. JOHN FAWCETT.	PAGE
Illustrating his Paper on Aspirations of a Pneumothorax under the X-Rays	52
Dr. ARTHUR F. HERTZ.	
Illustrating his Paper on Observations on a Case of Chyluria occurring in England	96
Mr. J. B. PARFITT.	
Illustrating his Paper on Mechanical Principles in Dentistry ... 140, 141, 142, 143, 144, 145, 146, 147	
Mr. RICHARD ASSHETON.	
Illustrating his Paper on Certain Features Characteristic of Teleostean Development 349, 352, 353, 355, 356, 358, 362, 364, 366, 369, 371, 376, 381, 383, 385, 386	
Dr. ARTHUR F. HERTZ.	
Illustrating his Paper on The Passage of Food along the Human Alimentary Canal 398, 404, 410, 417, 418, 419, 420, 421, 422, 424, 427	

CHARTS.

Dr. JOHN FAWCETT.	PAGE
Illustrating his Paper on Aspiration of a Pneumothorax under the X-Rays	51
Dr. J. W. H. EYRE.	
Illustrating his Paper on Micrococcus Melitensis and Antiserum 57, 59, 63, 66, 67	
Drs. M. G. LOUISSON and HERBERT FRENCH.	
Illustrating their Paper upon the Extent to which Vidal's Reaction persists after Recovery from Typhoid Fever	228

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Westminster Hospital Reports

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OBSERVATIONS UPON CHEYNE-STOKES' RESPIRATION.

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*A case of Cheyne-Stokes' respiration with incontinence
of urine due to a cerebral lesion lasting for four months.*

PART I.—OBSERVATIONS UPON THE RESULTS OF THE CLINICAL AND POST-MORTEM EXAMINATION. BY G. NEWTON PITT.

Thomas G—, aged 43, admitted October 3rd, 1904, on account of pain in his chest and of shortness of breath.

He was abroad in the army from 1881 to 1887. He had typhoid fever in 1884, but he has never had rheumatic fever. In May, 1904, he was under treatment for bronchitis and pain over his heart. He developed an attack in which he temporarily lost the use of his left arm, it became so feeble that he had to lift it up with his right

hand when he wished to move it. He himself attributed the weakness in his arm to over-use during his work as an electric car driver. He says there was also some slight difficulty in his speech, but these symptoms were only temporary. About ten days before admission he complained of pain in his chest and was very short of breath on walking or going upstairs, and there was some slight œdema of the legs.

Condition on admission.—He is a well-developed, healthy-looking man. On examination his lungs are found to be normal. The apex beat is in the fifth and sixth spaces one inch external to the nipple. The deep cardiac dulness begins above with the third rib. There is no dulness to the right of the sternum. A well-marked diastolic bruit is audible at the base of the heart traceable down the sternum. It is loudest in the second right space and up towards the neck. A systolic thrill is also palpable at the base. The urine is normal and is of sp. gr. 1020.

October 7th.—At 7.30 a.m. he felt faint and fell back on his pillow but did not completely lose consciousness. It was noted shortly after that his left arm and leg were paralysed, and to a less extent, the muscles on the left side of the face. The knee jerk on the left side disappeared, and the plantar reflex was in type extensor, while that on the right was flexor. The left lower extremity lay rotated outwards. There was incontinence of both urine and fæces, and he developed a Cheyne-Stokes' type of respiration. In the afternoon the paralysis diminished so that he was able to move his toes and foot on the left side and he regained some use in his left arm, having a fair grip. His mental condition is very dull, he lies in an indifferent semi-somnolent state.

10th.—The patient has improved considerably; he has regained the use of his left arm and leg, but he complains of abnormal sensation in them. His temperature has been normal, the grip of his hand is fair, and his mental condition has also improved.

12th.—The patient is restless and tries to get out of bed

at night. Sometimes there is considerable trouble in managing him. He has incontinence of urine two or three times a day, and also of fæces. He complains of some pain in the abdomen. He has been taking a mixture of 15 minims of tincture of digitalis and 7 grains of citrate of caffeine. The heart's action is feeble, the left ventricle dilated, and the compensation imperfect. The pulse is water-hammer in type. The paralysis was considered to be due to a small embolus in the right middle cerebral artery, with only a very small patch of softening. For some time it has been noticed that his hands are very livid, and apt to be cold.

26th.—The rhythmical character of the breathing remains very marked, but the power in the limbs of the left side is better. There is great mental torpor. He answers questions very slowly and deliberately in a sleepy sort of way, but accurately, and he moves his hands slowly. His pulse has become more irregular, the diastolic bruit is somewhat musical in character, and at the base of the heart there is a systolic bruit. The apex beat can be felt six inches from the sternum. Three grains of iodide of potassium were added to the mixture. The evidence pointed to the aortic incompetence being probably associated with atheroma of the aorta. During the variations in respiration it was noted that the size of the heart varied greatly. During dyspnoea there was no dulness to the right of the sternum, but with development of apnoea the right auricle became distended, so that on more than one occasion there was over an inch of dulness in the fourth right space. The characters of the Cheyne-Stokes' respiration are described later on by Dr. Pembrey and Mr. Allen.

November 4th.—His mental condition has slightly improved. There is still a little imperfection in sensation in the left leg, and a very slight paralysis persists.

17th.—The Cheyne-Stokes' respiration has persisted throughout, the depth of the respiration varying in a most marked way during the course of each minute. He has periods of fairly rapid deep-laboured respirations, which

gradually waxed and increased in intensity, their intensity then gradually diminishes, and this is followed by a period of apnœa of considerable duration in which there is but little or no respiratory movement. The respirations again start gradually increasing in intensity to be again vigorous for a short time. He remains in a drowsy condition, paying but little attention to his surroundings, and his talk is very often quite irrelevant; he can, however, be roused when he is able to answer a question properly. At times he is noisy and restless, especially at night. The incontinence persists, he is rather more anæmic than he was. A leucocyte count was 7000 per c.mm. The evidence has always been in favour of an atheromatous aorta, rather than of a fungating endocarditis. The temperature remains normal.

The right side of the heart became dilated during the periods of apnœa, and we were able on many occasions to demonstrate that, while in dyspnœa there was no dulness to the right of the sternum, during apnœa an area of dulness could be demonstrated extending as much as one inch and a quarter in the fourth space to the right of the sternum. Repeated observations were made with regard to the variation in his mental activity with the alterations in respiration; sometimes the latent period which elapsed before he said he felt a cutaneous stimulus was longer during apnœa than during dyspnœa. It was more difficult also to make him answer during apnœa, but on many occasions we were not able to satisfy ourselves of any appreciable difference in his mental activity during the two periods, and what difference there was, was more marked some days than it was others. No oscillatory movements of the eyes were noticed. The rate of pulse varied, but there was no marked difference in muscular power.

24th.—The urine contains a faint trace of albumen, having hitherto been free from it. The specific gravity varies from 1014 to 1028; a systolic thrill is often palpable at the base of the heart.

December 1st.—His condition has markedly changed, and is very grave to-day; his breathing is much more laboured, his hands and face are markedly cyanosed, and he is quite unconscious. The Cheyne-Stokes' respiration is more marked during sleep; he is unable to swallow food, which tends to pass into the trachea and set up choking. He is therefore fed with a nasal tube every eight hours. His temp. is 96° , his resp. 16, his pulse 70. While he was asleep it was noticed that the apnœa lasted about thirty-five seconds, and the dyspnœa about twenty-five, and these periods have been fairly constant. During the dyspnœa he took fifteen breaths; the thoracic movements commenced feebly, rose up to a maximum at the seventh, and then gradually died away again. The pupils are equal, and react to light both during the dyspnœa and the apnœa.

2nd.—The pupils remain equal in size. All day yesterday he did not speak; he was drowsy and unable to swallow. There were tracheal râles. He was very helpless, and the paresis in the left arm and leg were quite marked. About 2 p.m. he improved so that he was able to answer questions and to swallow. He was able to pick up a sixpence with his left hand, only very clumsily and with difficulty. His left thigh was rotated outwards, there was an extensor plantar reflex on that side, and the knee-jerk was brisker than on the right. The soft palate does not move when it is touched, but it does with phonation. His mental condition is not so good as previously, and he wanders more in his talk. He has the idea that he has been getting up for some days although he has not left his bed. The dyspnœa is very marked, and he is very restless. The pulse tracing is typical of aortic incompetence, with the vessel almost empty during diastole. His condition is feeble, so that he is unable to sit up in bed, and incontinence of urine and fæces still persist. He is still fed through the nose, and is taking a mixture containing digitalis, nitro-glycerine, and acetate of potash, and also a stimulating mixture

6 *Observations upon Cheyne-Stokes' Respiration.*

with some strychnine. The periods of dyspnœa and apnœa remain very fairly constant, as shown by the following table :

PERIOD OF DYSPNŒA.				APNŒA.
No. of respirations.		Duration.		Duration.
20	...	38 secs.	...	32 secs.
23	...	40	...	30
23	...	35	...	35
22	...	35	...	35
22	...	35	...	35
21	...	35	...	38
22	...	37	...	40
21	...	40	...	33
21	...	37	...	38

8th.—The nasal feeding was stopped on the 6th as he has been able to swallow since then, otherwise his condition remains unchanged, and he is still very dull mentally. His tongue is dry and furred.

15th.—He is taking his food better, and is able to use his left hand a little, and mentally he is so far improved that he can recollect events of two years ago. He still remains cyanosed. The systolic bruit at the base is still very rough.

18th.—He was able to be lifted on to a couch in the afternoon for a short time.

27th.—His mental condition has improved slightly, he has had less incontinence lately, and there is less cyanosis of his face and hands.

January 3rd, 1905.—The patient is more sensible, and talks rationally. There is a musical diastolic bruit audible and palpable over the cardiac area. The urine is sp. gr. 1010, and free from any abnormal constituents. The Cheyne-Stokes character of the breathing is less marked. The grip of his left hand is stronger, but it is necessary for him to concentrate his attention if he is to hold anything in it, as directly his attention is diverted the grip is relaxed.

20th.—The dyspnœa is greatly increased by fog. There is a slight trace of albumen in the urine.

On the 24th he was apparently in his usual condition, when at 1.30 p.m. he became extremely low and dyspnœic, the periods of dyspnœa greatly increasing in length. Towards the end he had a period of apnœa for ninety-seven seconds, followed by a period of dyspnœa, to die away again finally. The heart-sounds towards the end were more feeble and rapid, he became very cyanosed, and died after an attack which lasted half an hour in spite of treatment by strychnine and oxygen.

POST-MORTEM INSPECTION.

Old adhesions on the right side between the lobes of the lung, with general thickening of the pleura. The lungs were emphysematous.

Heart weighed 751 grammes. The left ventricle was considerably dilated, and its wall hypertrophied, the enlargement of the organ being mostly due to the change in this part.

The posterior aortic cusps were much atrophied, and the free edges thickened and retroverted, so as to allow an extreme amount of regurgitation. The endocardium immediately below the valves was thickened by the repeated impact of the regurgitant stream. The mitral valves, as also those of the right side, were normal.

The mitral orifice measured four inches, and the tricuspid five inches in circumference. The heart muscle appeared healthy.

The aorta was very atheromatous in its ascending portion, less so in the transverse portion of the arch. There was nothing specially characteristic of syphilis about it. The liver and alimentary canal were normal, the spleen weighed 280 grammes, and contained an old infarct. All the viscera were tough from chronic cardiac failure; the kidneys, weighing 368 grammes, appeared normal, excepting for the presence of three or four old shrunken infarcts. The testicles were healthy.

The brain weighed 1350 grammes. On inspection there was a large depression on the right side practically limited to the temporo-sphenoidal lobes, due to shrinking and softening of the cortex and subjacent tissues. The surface of the brain otherwise appeared normal. The whole of the second convolution, the anterior part of

FIG. 1.



A transverse section through right half of brain, showing area of softening shaded horizontally. The oblique shading indicates the site of a cavity where the softening had been extreme.

the first, and only a small anterior portion of the third, were softened.

The softening extends deeply, involving besides the cortex, part of the caudate, lenticular and optic thalamus ganglia, and the subcortical fibres; but only a small area in the anterior part of the internal capsule was involved. The rest of the brain was free from any softening, the left side being quite normal.

A series of transverse vertical sections were made with the following results :

(A) 6·5 cm. from the front (No. 3 Daniell's sections). This was just anterior to the tip of the temporo-sphenoidal lobes, and was free from disease.

B) 7·5 cm. (No. 5). The greater part of the lenticular nucleus and a small portion of the internal capsule are

FIG. 2.



A similar section, 2 cm. posterior to Fig. 1, through corpora mammillaria.

so extensively softened that their site is now occupied by an irregular cavity, which, however, is very much smaller than the area indicated in the diagram (Fig. 1) because the affected tissue has been greatly reduced in volume. The insular cortex and the outer part of the caudate nucleus are only partially softened. The lower corner of the lenticular nucleus is the only part of it which has escaped.

(c) 9·5 cm. (No. 9). Through the corpora mammillaria. In this section (Fig. 2) the tissues are soft but have not

broken down into cavities. The parts mainly affected are the first and second temporo-sphenoidal lobes, with the insula, the external capsule, and, to a less extent, the upper part of the lenticular nucleus. The first temporal convolution was less involved than the second. The corpus callosum, the optic thalamus, and the third temporal convolution, and the gyrus Hippocampi were unaffected.

The cerebral vessels showed some atheroma but no clot was detected in the right middle cerebral artery. There is no doubt the lower branches of the right middle cerebral artery were blocked, but whether due to an embolus or a thrombus still remains uncertain.

The result of the microscopical examination of the medulla is given later on.

Remarks.—The case presents several very remarkable features which may be discussed in turn. The patient, who had well-marked aortic incompetence, was seized on October 7th with an attack of left hemiplegia with incontinence of urine and fæces, and within a very short time development of a well-marked Cheyne-Stokes' respiration. The hemiplegia rapidly diminished so that on many occasions it was difficult to demonstrate it, although when he became very feeble it again became more obvious. The incontinence of urine, however, persisted more or less permanently, and was quite out of proportion to the amount of mental torpor which he exhibited and this raised the question as to whether it was due to a lesion of some cerebral centre or centres for the regulation of the function of the bladder. Bechterew,¹ in 1888, thought that there was a centre for micturition on the inner side of the anterior part of the optic thalamus. Czylharz and Marburg² in 1901 concluded that there were three cerebral centres for micturition—1. In the motor cortex at the junction of the centres regulating the movements of the upper and the lower extremities. 2. In the

¹ Bechterew, 'Neurolog. Centralblatt,' 1888, p. 505.

² Czylharz and Marburg, 'Jahrbuch f. Psychiatrie,' 1901.

corpus striatum: both of these serving for conscious automatic micturition. 3. A third centre in the optic thalamus which is actuated by the emotions over the bladder, and possibly also the cerebellum has some control. Lesions in the cortex and motor tracts produce retention, while those in the sub-cortical and cerebellar regions produce incontinence. The impulses are conveyed mainly by the pyramidal tracts.

Homburger,¹ who in 1903 re-investigated the whole subject, does not agree with them, but came to the conclusion that a unilateral patch of softening in the basal ganglia only causes a transitory incontinence, but the patient soon learns to keep clean in the daytime although the act of micturition may often be precipitate; incontinence would, however, often occur in the night. With the development of a second patch of softening in the ganglia on the opposite side with or without a lesion of the direct cortical capsular fibres, the incontinence became permanent and was indistinguishable from a spinal incontinence, the urine constantly dribbling away. There would also generally be some residual urine, and micturition was always so precipitate that although there might be a sensation of the need to micturate there was usually not time to obtain a vessel to catch the urine. In addition to incontinence, bilateral lesions of the ganglia produced spasmodic paraparesis of the lower extremities, with retention of the movements of the feet and inability to pass from the recumbent to the sitting posture, exaggerated reflexes, an absence of Babinski's reflex and spasmodic attacks of laughing and weeping. When the patient was sat up on a chair, his legs would be stretched out stiffly in front of him, his head would be sunken on his chest and he would slip off the chair if not held. When he tried to walk it was as if on stilts with his legs wide apart, and the power in the arms was not perfect. Homburger collected ten cases of multiple softening of the ganglia, in six of which the lesions were bilateral and the incontinence was persistent.

¹ A. Homburger, 'Neurolog. Centralblatt,' 1903, p. 199.

He selected cases in which the cortex and internal capsule were unaffected. Lesions below the floor of the ganglia did not give rise to these symptoms. He came to the conclusion that superficial cortical lesions did not produce a permanent incontinence of urine, whereas bilateral lesions of the sub-cortical fibres and basal ganglia will do so. The lesion in the present case was in the ganglia on the right side and extended out to the surface of the brain below the Sylvian fissure, the damage above this being extremely minute. No lesion whatever could be discovered on the left side of the brain. The incontinence, although somewhat persistent, was not as marked and continuous as in the cases Homburger described when there were bilateral lesions. The incontinence was undoubtedly more marked and persistent than we have met with in other cases of hemiplegia, especially bearing in mind that although he was slow his mental condition was often very fair and the amount of paralysis very slight. Still while it might be brought forward as evidence supporting Czynharz and Marburg it cannot be said to really controvert Homburger's conclusions.

The cases of softening which Homburger considered were due to degenerate arteries were multiple, hence the frequency with which the lesions were bilateral; but in the present case the area of softening was a very extensive one and was due to an embolus, the opposite side of the brain being healthy. Although it was noted that the patient was unable to sit up unless supported, he presented no other evidence suggestive of a bilateral softening of the ganglia.

PART II.—EXPERIMENTAL OBSERVATIONS, ESPECIALLY IN
RELATION TO THE CAUSATION OF PERIODIC BREATHING.
BY M. S. PEMBREY AND R. W. ALLEN.

The phenomena of Cheyne-Stokes' respiration were presented by the patient in so pronounced a form that it seemed important to determine, if it were possible, the

cause or causes of the periodic breathing. The problems which needed investigation were the apnœa, the period of waxing and waning respiration, and the relationship of these to each other, and to any changes in the circulation and nervous system. The apnœa might be due to the removal of so much carbon dioxide from the blood by the previous deep and rapid breathing that the partial pressure of the gas was depressed below its stimulating value for the respiratory centre; on the other hand apnœa might arise from the absorption of sufficient oxygen during the period of breathing to maintain the pressure of oxygen in the blood above the value at which deficiency of oxygen arouses the nerve-cells of the respiratory centre. Further, it might be that both of these changes were involved in the production of apnœa. The typical waxing of the respiratory movements during the period of breathing might be due to an increase of carbon dioxide, a decrease of oxygen, or to both of these factors.

Such were the causes to be sought on the theory that apnœa and breathing are due to changes in the tensions or partial pressures of the gases in the blood which supplies the respiratory centre in the medulla. There are, however, other possible factors. The periodic breathing might be due to intrinsic rhythmic changes in the activity of the nerve-cells of the centre for respiration. The rapid and deep ventilation of the lungs during the dyspnœa might, by impulses sent up the vagus nerves, so alter the excitability of the centre that respiration would be inhibited for a period. Rhythmic changes in the contraction of the heart and the circulation of the blood might cause alternating periods of activity and inactivity in the nerve-cells of the respiratory centre. These views were kept in mind, but attention was chiefly directed to the regulation of the respiratory movements by the gaseous constituents of the arterial blood for experiments upon men and animals show that the partial pressures of the carbon dioxide and oxygen are the most important factors.

The respiratory movements.—The Cheyne-Stokes' breath-

ing was observed fifteen weeks before the death of the patient, and, apart from a few days on which continuous or irregular respiration was noted, it persisted during that time. The period of apnœa lasted twenty to forty seconds, and during the phase of breathing there was a typical waxing and waning of the respiratory movements. The first breath which followed the apnœa was so slight as to need careful observation for its detection; it was succeeded by a series of respirations increasing in depth and culminating in deep gasping breaths; these gradually decreased in amplitude and died away into the next period of apnœa. The phase of breathing lasted about forty seconds; the cycle, therefore, occupied about one minute.

The alternation of breathing and apnœa persisted for hours or even days; changes, indeed, were observed in the duration of the respective periods on different days, but on any given occasion the time relations were often very constant. The character and duration of the respiratory movements are well shown by the graphic records (Plates: Figs. I, II, IV, VI, XI), and the following determinations are samples of which others are given in the appendix to this paper or recorded graphically in the curves.

Date.		Duration of apnœa in seconds.		Duration of breathing in seconds.		Number of respirations.
Nov. 26, '04	...	27	...	45	...	20
		25	...	47	...	27
		26	...	47	...	28
		26	...	47	...	27
		26	...	45	...	26
		30	...	47	...	27
Dec. 2, '04	...	36	...	34	...	20
		35	...	37	...	22
		36	...	37	...	20
		32	...	31	...	21
		38	...	35	...	20
		37	...	36	...	20
Jan. 11, '05	...	18	...	50	...	26
		21	...	43	...	28
		22	...	44	...	22

The ventilation of the lungs during the Cheyne-Stokes' breathing was determined by allowing the patient to breathe through a mask provided with inspiratory and expiratory valves, and connected with a gas-meter. The volume of air expired was between six and seven litres per minute, and a similar value was obtained when the patient was feeling better in health, and was breathing continuously. It follows, therefore, that an excessive ventilation of the lungs was effected by the forcible respirations of the periodic breathing; a larger quantity of oxygen than normal would thus be brought into the alveolar air, and a larger quantity of carbon dioxide would be removed. This effect, however, would be of a temporary nature. At the end of apnœa the composition of the alveolar air would show an opposite condition, and thus there would be, during a complete cycle, an oscillation between two extremes. This alternation will be demonstrated later by the analyses of the samples of alveolar air which were taken at different phases of the Cheyne-Stokes' breathing.

The variations in the volumes of the expirations during the waxing and waning respiration are shown by the following figures: 10, 20, 40, 250, 340, 100, 100, and 150 c.c. These were recorded when the patient breathed 21·2 litres of air in three minutes and twenty-nine seconds, that is at the rate of 6·1 litres per minute.

The heart, pulse, and blood-pressure.—The influence of the respiratory movements upon the pulmonary circulation is well shown by the difference in the area of cardiac dulness on the right side during the alternating periods of breathing and apnœa; the respiratory movements favour the passage of the blood from the right to the left side of the heart, and their cessation during apnœa was accompanied by an increase of cardiac dulness to the extent of an inch or more in the fourth intercostal space to the right of the sternum. The rate of the pulse was irregular, but, as the following determinations show, was generally more rapid during the period of apnœa:—

16 *Observations upon Cheyne-Stokes' Respiration.*

Date.	Apnœa, duration in seconds.	Pulse beats, actual.	Pulse rate per minute.	Hyperpnœa, duration in seconds.	Pulse beats, actual.	Pulse rate per minute.	Number of respi- rations.
	33 ...	48 ...	87 ...	37 ...	52 ...	84 ...	—
	31 ...	47 ...	91 ...	40 ...	52 ...	78 ...	—
	32 ...	48 ...	90 ...	35 ...	50 ...	86 ...	—
	33 ...	50 ...	91 ...	38 ...	50 ...	79 ...	—
	34 ...	50 ...	88 ...	40 ...	53 ...	80 ...	—
Nov. 26, '04 ...	27 ...	36 ...	80 ...	45 ...	60 ...	80 ...	29
	25 ...	37 ...	89 ...	47 ...	59 ...	75 ...	27
	26 ...	38 ...	88 ...	47 ...	61 ...	78 ...	28
	26 ...	33 ...	76 ...	47 ...	60 ...	77 ...	27
	26 ...	32? ...	74? ...	45 ...	60 ...	80 ...	26
	30 ...	39 ...	78 ...	47 ...	62 ...	79 ...	27

In each of the above series the periods are consecutive.

The blood-pressure in the brachial artery was determined by C. J. Martin's modification of the Riva Rocci sphygmometer,¹ and it was found to rise during the period of breathing. At the end of apnœa and the beginning of breathing the pressures observed in three determinations were 175, 175, and 170 mm. of mercury. At the end of the period of breathing and the beginning of apnœa the respective values were 195, 195, and 190 mm. of mercury. These figures represent the maximum pressure, for, owing to the incompetence of the aortic valves, the mean pressure was low.

The composition of the air in the alveoli of the lungs during the different phases of the period of breathing.—There is no doubt that the gaseous composition of the blood which supplies the brain regulates the depth and frequency of the respiratory movements; other factors there may be, and probably are, but the condition of the arterial blood is the most important. An increase in the partial pressure of the carbon dioxide increases the depth and frequency of respiration; a decrease in the pressure of oxygen will have a similar effect, but one which is relatively not so marked. It is impossible, except in the

¹ The apparatus used gave for the blood-pressure of healthy men at rest values of 100 to 110 mm. of mercury.

case of animals, to obtain samples of the blood flowing to and from the brain, or to measure the rapidity of the circulation. A determination, however, of the composition of the alveolar air of the lungs may give some idea of the pressures of the gaseous constituents of the blood which is flowing into the left auricle, and thence through the left ventricle, aorta and its branches to the brain. The blood in the pulmonary capillaries is separated from the air in the alveoli by a layer of tissue only 0.001 mm. thick, and the total area of the capillaries is so enormous that the blood may be considered as a vast sheet of fluid exposed to the alveolar air over a surface of 90 square metres. Equality of pressure between the gases of the blood and alveolar air would thus be facilitated, and is, indeed, believed by many physiologists to occur.

The exactness of such an indirect estimation of the pressures of carbon dioxide and oxygen in the arterial blood cannot be stated. If, as Pflüger, Zuntz, Loewy, and others maintain, the gaseous transference between the blood and the air in the alveoli of the lungs depends upon the differences in the partial pressures of the component gases in the blood and alveolar air, then an analysis of the alveolar air will yield a measurement of the pressures of the gases in the blood flowing in the pulmonary capillaries; if, on the other hand, as Bohr and Haldane believe, the pulmonary epithelium can secrete oxygen from a lower pressure in the alveolar air to a higher pressure in the blood, it follows that such results for oxygen at least may be misleading. A deficiency of oxygen, according to Bohr, Haldane, and Lorrain Smith, stimulates the pulmonary epithelium to greater secretory activity. The discharge of carbon dioxide is, according to Bohr, an active excretory process, for he finds that the pressure of the gas in the arterial blood may be below the partial pressure of the gas in the alveoli. This difficult question cannot be decided, for there is at present no evidence which is accepted as conclusive; it is unnecessary to discuss it here, especially since the evidence for

and against the rival theories has been recently given elsewhere.¹

Samples of the alveolar air at different stages of the waxing and waning respiration were taken by the method employed by Haldane and Priestley; a modification was necessary in the shape of a mask, which fitted in an air-tight manner over the patient's nose and mouth. The results of the analyses are given in the following table.

*Composition of the Alveolar Air.*²

Early Period of Waxing Respiration.

Date.		Number of expiration.		Carbon dioxide vols. per cent.		Oxygen vols. per cent.
Nov. 25, '04	...	3rd	...	3.90	...	12.19
		3rd	...	3.61	...	12.84
Dec. 6, '04	...	2nd	...	3.56	...	13.61
		3rd	...	3.63	...	13.66

Period of Dyspnœa.

Date.		Number of expiration.		Carbon dioxide vols. per cent.		Oxygen vols. per cent.
Nov. 25, '04	...	5th	...	3.26	...	15.48
		10th	...	2.76	...	17.60
Dec. 6, '04	...	8th	...	3.22	...	15.67
		10th	...	2.97	...	16.66
		12th	...	2.74	...	16.75

Late Period of Waning Respiration.

Date.		Number of expiration.		Carbon dioxide vols. per cent.		Oxygen vols. per cent.
Nov. 25, '04	...	23rd or 24th	...	2.93	...	17.49
		24th	...	2.63	...	18.5
Dec. 6, '04	...	18th	...	2.00	...	18.86

In the cases of the early period of waxing and the late period of waning respiration the true values for the carbon dioxide are, no doubt, higher, and for the oxygen lower, owing to the shallow nature of the first and last expira-

¹ Article "Respiratory Exchange," by M. S. Pembrey, 'Recent Advances in Physiology and Bio-Chemistry,' edited by L. Hill, 1906.

² The alveolar air was measured saturated with water at 10°–14° C. Haldane's apparatus for gas analysis was used.

tions. The alveoli of the lungs are the effective seat of gaseous interchange; the remaining space, extending from the nose through the pharynx, larynx, trachea, bronchi, and bronchioles, is known as the "dead space." According to the estimations of Loewy, Haldane, and Priestley the "dead space" of the respiratory tract is about 140 c.c. The last portion of the air expired in a shallow expiration would thus be an admixture of air from the "dead space" and the alveoli, for it has already been mentioned that the volume of the air expired at different phases of the periodic breathing varied from 10 to over 340 c.c. The average volume of an expiration was 193 c.c. during a period of five minutes, when the patient took 179 breaths and expired 34·75 litres of air.

When the patient's general condition was better, and his breathing was of the continuous type, 31 per minute, the percentage composition of the alveolar air was 4·44 vols. of carbon dioxide and 16·34 vols. of oxygen; after the return of Cheyne-Stokes' respiration on this occasion the composition of the sample taken from the third expiration of the waxing breathing was 4·91 per cent. of carbon dioxide and 13·97 per cent. of oxygen.

The table of analyses shows that the partial pressure of carbon dioxide in the alveolar air was highest at the end of apnœa, and gradually decreased during the period of breathing; the partial pressure of oxygen showed a reverse relationship, and was highest at the end of the rapid breathing. The percentages of oxygen in the samples at the end of apnœa are so low that, according to Loewy's observations, the respiratory centre would be stimulated by the deficiency of oxygen. It would therefore appear that the carbon dioxide accumulates and the oxygen diminishes, until at last the nerve-cells of the respiratory centre are stimulated, the waxing respirations begin and culminate in very deep and rapid respirations, whereby much carbon dioxide is washed out and a large quantity of oxygen is taken in; apnœa then follows, due apparently to the absence of sufficient carbon dioxide to

stimulate the nerve-cells. The cycle would then be repeated.

It has long been known that apnœa can be readily produced in a healthy man by a series of rapid and deep breaths. By such an experiment an artificial condition of breathing, somewhat resembling Cheyne-Stokes' respiration, can be maintained for a time. The following analyses give the composition of the alveolar air at different phases of such experiments.

Experiments upon healthy men.—Subject: R. W. A.— Analyses of alveolar air, second expiration of waxing respiration—carbon dioxide 5·79 per cent., oxygen 12·24 per cent.; eighth expiration at height of deep and rapid breathing—carbon dioxide 4·16 per cent., oxygen 17·29 per cent.

Subject: M. S. P.— Breathed rapidly and deeply 18 times in 20 seconds, then breathed out a sample of alveolar air—carbon dioxide 3·22 per cent., oxygen 19·21 per cent.

Subject: M. S. P.— Breathed rapidly and deeply 17 times in 18 seconds. Sample of alveolar air from the last expiration—carbon dioxide 2·50 per cent., oxygen 19·23 per cent. Apnœa followed. The sample of the first expiration, when a desire to breathe was felt, had the following composition—carbon dioxide 5·59 per cent., oxygen 12·59 per cent.

Subject: A. B.— Breathed rapidly and deeply 21 times in about 20 seconds. Sample of alveolar air from the last expiration—carbon dioxide 4·10 per cent., oxygen 18·29 per cent. Apnœa followed. The sample of the first expiration, when a desire to breathe was felt, had the following composition—carbon dioxide 6·11 per cent., oxygen 11·26 per cent.

The results of the analyses of the alveolar air lead to the conclusion that the periodic breathing is probably due to changes in the partial pressures of the oxygen and carbon dioxide of the arterial blood which supplies the respiratory centre. In order to test this view observations were made upon the influence of various percentages of oxygen and carbon dioxide in the air which the patient breathed.

The influence of various percentages of oxygen upon the

respiration.—The observations were carried out by allowing the patient to breathe oxygen which was supplied through a mask provided with inspiratory and expiratory valves. The respiratory movements were recorded graphically for long periods upon a large kymograph, which carried a piece of smoked paper 280 cm. long and 25 cm. wide; such long records were necessary in order to control the observations. The procedure was as follows:—A stethograph, consisting of a small rubber bag, was fastened round the patient's waist at the level which gave the most movement during the weaker contractions of the diaphragm, and was connected with a recording tambour by means of flexible leaden tubing; it was thus possible to replace the bedclothes and, without any disturbance of the patient, to record the respiration for an hour or two; on some occasions the patient even went to sleep during the observations. The stethograph was sensitive enough to record, if it were required, the contractions of the heart as well as the respiratory movements. A record of the respiration of the patient was taken when he was lying quite undisturbed in bed; this part will be called in the description of the tracings "the control without mask and valves." During the continuation of the record the mask provided with inspiratory and expiratory valves was applied to the patient's face; the invariable effect was at first a shortening or abolition of the period of apnœa, but this soon passed off, and Cheyne-Stokes' respiration reappeared; this part of the observation will be designated "the control with mask and valves." Oxygen was then delivered from a cylinder into a rubber bag, which was connected by a tube with the inlet of the mask; the gas could thus be supplied under a pressure so slight as not to force the inspiratory valve during the phase of apnœa.

The following series of tracings will show that almost pure oxygen (90 per cent.), inhaled through a mask provided with inspiratory and expiratory valves, produced a very definite effect; in about half a minute or more the periods of apnœa became shorter, then were filled in by

shallow respirations, and in about three or four minutes were completely abolished; easy respirations of a continuous type were obtained during the further administration of the gas. The supply of oxygen was discontinued, but for the purpose of control the mask and valves were retained in position; the continuous type of respiration persisted for about a minute, then shallower respirations ushered in the return of periodicity, and finally the typical Cheyne-Stokes' respiration was obtained. The mask was removed, and then, after a further record, the observation was brought to an end. Variations in the promptness of the effect are shown by the different curves (Plates: Figs. II, IV, V, VI).

On various occasions the following percentages of oxygen were administered, namely 89·97, 20·9, 17·43, 15·2, 14·38, and 8·67, and the tracings show that percentages above and below the amount of oxygen present in atmospheric air tended to abolish, or actually did abolish, the Cheyne-Stokes' respiration. When pure oxygen was inspired the respirations were easy, the patient felt more comfortable, and the dusky hue of the face was replaced by a more natural colour; when there was a deficiency of oxygen the respirations were deeper, but there was no distress (Plates: Figs. III, IX, X).

The administration of oxygen in the ordinary clinical way by a glass funnel held in front of the patient's face did not abolish the periodic breathing; this was probably due to the dilution of the oxygen with air.

The total volume of air expired when the patient was breathing air and exhibiting Cheyne-Stokes' breathing was greater than the volume expired when he was breathing pure oxygen by means of the mask and valves. Thus during three whole periods of typical periodic breathing lasting 240 seconds 29·5 litres of air were expired, a rate of 7·4 litres per minute; oxygen was given, and in the first period of 90 seconds 9 litres were expired, a rate of 6·0 litres per minute; the respiration became continuous in type, and during 420 seconds 44 litres were expired, a rate of

6.3 litres per minute ; the oxygen was replaced by air and Cheyne-Stokes' respiration returned, 18 litres were expired in 180 seconds, a rate of 6.0 litres per minute. A delay both in the appearance and the disappearance of the effect of oxygen upon the patient's breathing is shown in the tracings ; this would be expected, for not only would several seconds elapse before the air in the alveoli became rich in oxygen, but time would also be required for the passage of the blood through the lungs and thence to the capillary vessels of the medulla oblongata. According to G. N. Stewart's calculations the blood passes from the pulmonary artery through the lungs to the pulmonary veins in about 15 seconds.

The influence of various percentages of carbon dioxide upon the respiration.—The effect of carbon dioxide in air or oxygen was investigated in a similar manner to that just described for oxygen. The curves show that the effect of carbon dioxide in amounts above 2 per cent. was very definite and prompt ; with a low value, 2.26 per cent. in air, the apnœa was abolished but the waxing and waning respiration persisted ; with higher percentages all tendency to periodicity was abolished (Plates: Fig. xi). Carbon dioxide always yielded satisfactory results provided that it was above the minimum mentioned ; in this respect it was more certain than oxygen. When the administration of the gas was discontinued the periodic respiration quickly returned. These facts are so clearly demonstrated by the graphic records that no further account is necessary.

The expired air of the patient contained 2 to 3 per cent. of carbon dioxide, an amount which was always sufficient to abolish apnœa (Plates: Fig. viii). The tolerance of the patient to high percentages of carbon dioxide is shown by Plate Fig. vii, and will be discussed later.

The influence of psychical conditions upon the respiration.—It may be stated briefly that anything which tended to increase the nervous excitability of the patient shortened or abolished for a time the period of apnœa,

and lessened the severity of the dyspnœa. It was often necessary to prolong the records owing to the disturbance introduced by some one coming to the bed and discussing the patient's condition and respiration. The influence of suggestion upon the mind of the patient was carefully watched; not only were the controls without and with the mask and valves made during each observation, but the supply of oxygen was several times stopped without the knowledge of the patient and replaced by air; on other occasions the oxygen was allowed unknown to the patient to escape into the air of the ward, so that the noise caused as it issued from the cylinder into the bag might still continue when the patient was breathing air. Oxygen and air were also given from large wedge-shaped gas-bags for the purpose of control. When mixtures of carbon dioxide and various percentages of oxygen or air were administered, one or two large gas-bags were used, and the mixture, whatever it might be, was known to the patient only as gas.

During sleep there was a tendency for the Cheyne-Stokes' respiration to be more pronounced, and on days when the breathing was continuous the periodic respiration often returned during sleep. Movement of the head from side to side during each period of breathing was sometimes seen in the patient when he was asleep.

The patient's mental condition appeared to be more active during the period of breathing than in the period of apnœa, and he often showed more inclination to talk during that time. Conversation with the patient would tend to abolish apnœa. When his general condition was better the respiration was continuous. He could at other times by an effort of the will breathe continuously for a short time, but soon relapsed into periodic breathing (Plates: Fig. III).

The condition of the respiratory centre.—Stress has been laid upon the evidence of diminished nervous excitability, for all the observations tend to confirm the view that Cheyne-Stokes' breathing is associated with

a diminished excitability of the central nervous system. It is known that Cheyne-Stokes' respiration is present under perfectly natural conditions in mammals during some of the stages of hibernation, and in healthy infants and some adults during sleep; it can be produced in healthy animals by morphia and chloral. In these cases the general nervous excitability is diminished. During disease periodic breathing often follows the administration of morphia and chloral: in the present case such drugs were not given to the patient.

Confirmation of this view was found in the results obtained from the microscopic examination of the medulla oblongata. This was carried out by Dr. E. F. Buzzard, to whom we are greatly indebted for the excellent preparations and the following report:

Report on the Microscopic Examination of the Pons and Medulla oblongata. By E. F. Buzzard, M.A., M.D., F.R.C.P.

"The brain stem was hardened in 5 per cent. formalin. Three methods were employed in the examination of the pons and medulla.

(1) The Busch modification of the Marchi method for demonstrating recent degeneration in the nerve-fibres.

(2) A modified Nissl stain for investigating the condition of the nerve cells, and

(3) The ordinary hæmatoxylin-eosin stain for observing any morbid condition of the meninges or blood-vessels.

(1) *Busch method.*—A few sections from different levels of the pons and medulla were stained by this method and examined microscopically. A considerable number of fibres in the left, and a smaller number of fibres in the right pyramidal tracts were found to have undergone degeneration in all the sections, but the majority of the fibres in both were healthy.

With the exception of a few scattered degenerated fibres in the lateral regions of the medulla and in the tegmental region of the pons no other changes were observed.

(2) *Nissl method.*—The stain used was methylene blue, and a large number of sections were mounted serially from the posterior half of the fourth ventricle. It may be stated at once that the fixation and staining were very successful, and it was possible to study accurately the condition of the cells forming the nuclei of the 8th, 9th, 10th, and 12th cranial nerves.

(a) *The hypoglossal nucleus.*—The cells of this nucleus were of healthy size and shape on both sides. They

FIG. 3.



Nearly normal cell from the hypoglossal nucleus.

contained numerous chromatin granules which were rather larger than the normal, and in some instances tended to encroach upon the nucleus and render the latter less well defined than usual. The nucleolus was generally centrally situated, and rather prominent, perhaps slightly swollen.

On the whole the cells had a healthy appearance.

(b) *The dorsal nucleus of the vagus.*—In this case marked changes were seen in the cells, especially on the left side. In the left nucleus only about one third of the cells were of healthy appearance, and these were mostly situated in the ventral part of the nucleus. The remainder of the cells had undergone changes chiefly of

an atrophic character. Many were shrunk, greatly altered in shape, and contained only a few coarse granules with no recognisable nucleus or nucleolus. Others showed slight chromatolytic changes with excentric nuclei. Examples of the various types are represented in Figs. 4 and 5. It should be remembered that serial sections were examined, and it was possible therefore to examine the whole of each cell, and to exclude the possibility of the appearances being due to their incomplete presentation in any particular field. On the

FIG. 4.



FIG. 5.



FIG. 4.—Healthy cells from the left dorsal nucleus of the vagus, near its ventricular aspect.

FIG. 5.—Degenerate cells from the deeper portions of the left dorsal nucleus of the vagus.

right side the changes were similar in character, but did not involve so large a proportion of the cells.

(c) *The nucleus ambiguus*.—The cells of this nucleus were, on the whole, natural in size and general appearance, although one or two showed chromatolytic changes. No difference was noted between the cells of the right and left sides.

(d) *The fasciculus solitarius*.—The cells situated around this bundle were scanty, and many of them had undergone morbid changes which are represented in Fig. 6. Excentration of nuclei and chromatolysis were noticeable and were often associated with a considerable amount of pigmentation.

(e) *The nucleus of the descending root of the eighth nerve.*—A large number of the cells of this nucleus showed swelling, chromatolysis, and excentration of nuclei, but there were no atrophic changes similar to what was seen in the case of the dorsal nucleus of the vagus. Two cells showing varying degrees of change are represented in Fig. 7.

(3) *Hæmatoxylin-eosin method.*—Only a few celloidin sections were stained by this method, and no very marked changes were observed in the blood-vessels. Slight

FIG. 6.



FIG. 7.



FIG. 6.—Chromatolysis and pigmentation of cells of the descending glossopharyngeal root.

FIG. 7.—Slightly changed cells (chromatolysis) from the descending vestibular root.

thickening of the meninges with a small excess of round cells and numerous corpora amylacea were noted in some parts. No evidence of capillary thrombosis or hæmorrhage was forthcoming.

In conclusion it may be said that the most profound changes were seen in the dorsal nucleus of the vagus where a large proportion of the cells, especially on the left side, had undergone marked atrophy and degeneration.

The alteration in other nuclei were mostly of the chromatolytic type such as is commonly seen in toxic con-

ditions or as a reaction to lesions in the axis cylinder processes."

We may regard these changes in the pons and medulla oblongata, as well as those already described in the cerebrum, as due to defective supply of arterial blood. Experimentally such changes have been produced by Mott and Leonard Hill.

DISCUSSION OF THE RESULTS.

It is now necessary to discuss the results and explain, if it be possible, the cause of Cheyne-Stokes' respiration. The examination of the patient gave evidence of diminished nervous excitability, which was probably caused by a defective supply of blood to the brain due to the aortic regurgitation and atheroma. It could be easily understood that the respiratory centre would be still excited by a deficiency of oxygen, if the partial pressure of carbon dioxide were below its stimulating value, or the abnormal centre were less sensitive to carbon dioxide, the usual stimulus to respiration. The following may be the sequence of events:—The partial pressure of the carbon dioxide increases and the oxygen decreases until the centre is stimulated, the respirations are feeble at first but gradually increase in vigour until they culminate in rapid deep respirations whereby a large quantity of carbon dioxide is washed out of the alveolar air and blood and a large quantity of oxygen is taken in. The respiratory centre is no longer stimulated owing to the reduction in the partial pressure of carbon dioxide and the increase in oxygen, apnoea therefore follows and persists until the cycle begins again. Owing to the time taken for the passage of the blood through the lungs to the medulla oblongata, there will be some delay before the effect of the pulmonary ventilation can be shown upon the respiratory centre; thus will arise the waxing and waning of respiration. The volume of the first breath or two

during the period of breathing is so small that it will have no effect upon the composition of the alveolar air and the strength of the stimulus to the respiratory centre will be increasing meanwhile.

If these views be correct, the administration of carbon dioxide by increasing the partial pressure of the gas in the alveolar air and arterial blood should supply a constant stimulus to the respiratory centre and apnœa should cease. The graphic records show that the inhalation of carbon dioxide in percentages varying from 2·2 to 11·2 produced all gradations from feeble respirations in the place of apnœa to continuous breathing of almost regular type. A small percentage of carbon dioxide, 0·76, as would be expected, was not enough to raise the partial pressure of the gas to its stimulating value. Further, if the partial pressure of the carbon dioxide in the arterial blood be low during Cheyne-Stokes' breathing and the nervous excitability of the respiratory centre diminished, the patient should tolerate a greater dose of carbon dioxide than can a healthy man. This was found to be the case, air containing 11·2 per cent. of carbon dioxide produced regular breathing in the patient but great distress in ourselves. The administration of carbon dioxide would also probably improve the circulation by its stimulating action upon the heart.

The analyses of the alveolar air showed that the percentage of oxygen was sufficiently low at the beginning of the period of breathing to produce excitation of the respiratory centre. It is also necessary to consider why the administration of oxygen abolished the Cheyne-Stokes' respiration. It would seem that the breathing of the pure oxygen by the mask and valves maintained the pressure of oxygen in the alveoli and the blood at such a high level that, notwithstanding the aortic regurgitation, the respiratory centre was well supplied with oxygen, and being no longer stimulated by a deficiency of the gas, did not send out the vigorous impulses which had previously resulted in rapid deep breathing, whereby much carbon

dioxide had been washed out of the alveoli and blood at the same time that oxygen was taken in. The partial pressure of the carbon dioxide would thus be maintained at a more constant level, and would stimulate the respiratory centre to regular rhythmic activity. In order to test this view, samples of alveolar air were taken soon after the patient had breathed pure oxygen; the fifth expiration after the inhalation of oxygen gave 3·47 per cent. carbon dioxide, and 24·71 per cent. oxygen, the twenty-second expiration yielded a sample with 4·31 per cent. carbon dioxide, and 17·26 per cent. oxygen. Moreover, the natural continuous breathing of the patient yielded on different occasions samples of alveolar air with the following percentage compositions:—Carbon dioxide 4·27, 3·52, 4·44, oxygen 15·00, 15·7, 16·34.

The increase in the percentage of carbon dioxide is not very great, but, considered in relation to the percentage of oxygen, the difference between the alveolar air of continuous and periodic breathing is more accentuated.

It has been shown that the inhalation of a mixture of oxygen and nitrogen containing a smaller percentage of oxygen than that present in atmospheric air also abolished apnoea. The explanation is, doubtless, that there was a constant deficiency of oxygen, and thus a continual stimulus to the nerve-cells of the respiratory centre.

The continuous respiration produced by voluntary effort or slight excitement of the patient appears to have been due to an increase in the excitability of the respiratory centre caused by nervous impulses passing from higher centres to the neurons of the centre in the medulla.

CONCLUSIONS.

It would appear that the periodicity of Cheyne-Stokes' respiration in this case is due to a diminished excitability of the nervous system associated with a defective supply of arterial blood; the carbon dioxide accumulates, and

the oxygen diminishes until at last the nerve-cells are stimulated, the waxing respirations begin and culminate in marked dyspnœa, whereby a large quantity of carbon dioxide is washed out and sufficient oxygen is taken in; apnœa then follows, due, apparently, to the absence of sufficient carbon dioxide to stimulate the nerve-cells.

The inhalation of air containing more than 2 per cent. of carbon dioxide abolishes apnœa by maintaining the partial pressure of the carbon dioxide in the alveolar air and blood at its stimulating value.

The administration of pure oxygen by means of a mask and valves abolishes apnœa by maintaining the partial pressure of carbon dioxide in the blood at its stimulating value. The respiratory centre is no longer excited by lack of oxygen to send out the forcible impulses which had previously resulted in excessive ventilation of the lungs, whereby carbon dioxide had been washed out of the alveoli and blood.

Air containing a smaller percentage of oxygen than that present in atmospheric air abolishes apnœa; the constant deficiency of oxygen stimulates the respiratory centre.

REFERENCES.

No attempt has been made to examine the extensive literature on Cheyne-Stokes' respiration. The following articles either refer to questions raised in this paper or serve as a guide to the subject.

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CURLS (Gazz. degli Osped., Dec. 10th, 1905).—Epitome, p. 13. Brit. Med. Journ., Jan. 27th, 1906.

PEMBREY AND PITT.—Journ. Physiol., vol. xxiv, 1899, p. 305.

PEMBREY.—Ibid., vol. xxvii, 1901, p. 78.

APPENDIX.

The data of observations not already given are collected here in order that the paper may not be overloaded with tables of results.

Table to show the duration of apnoea and breathing on various days, and the number of respirations during the periods of breathing.

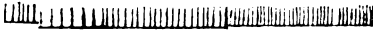
Date.	Duration of apnoea in seconds.		Duration of breathing in seconds.		Number of respirations.	
Dec. 1, '04	...	33	...	37	...	—
		32	...	40	...	—
		33	...	35	...	—
		34	...	38	...	—
		33	...	40	...	—
Dec. 13, '04	...	43	...	41	...	18
		38	...	40	...	18
		43	...	46	...	20
Dec. 14, '04	...	37	...	49	...	17
		28	...	45	...	18
Dec. 15, '04	...	23	...	40	...	17
		22	...	38	...	16
		19	...	40	...	18
		21	...	38	...	16

34 *Observations upon Cheyne-Stokes' Respiration.*

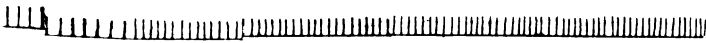
Date.		Duration of apnoea in seconds.		Duration of breathing in seconds.		Number of respirations.
Dec. 17, '04	...	18	...	42	...	18
		22	...	47	...	18
Dec. 20, '04	...	20	...	52	...	20
Dec. 21, '04	...	20	...	44	...	19
		18	...	49	...	19
		18	...	40	...	18
		19	...	38	...	15
Jan. 5, '05	...	15	...	43	...	20
		16	...	48	...	21
Jan. 10, '05	...	25	...	46	...	23
		22	...	49	...	24

Note.—A preliminary account of the observations made by Pembrey and Allen was communicated to the Physiological Society, January 21st, 1905 ("Proc. Physiol. Soc.," 'Journ. Physiol.,' vol. xxxii, 1905, p. 18).

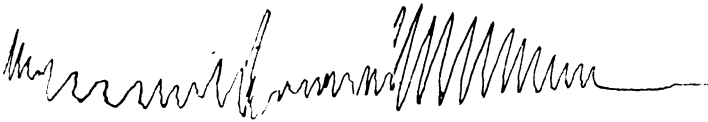
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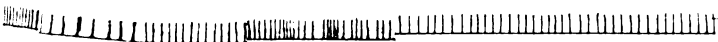
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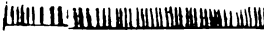


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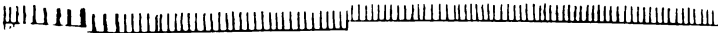
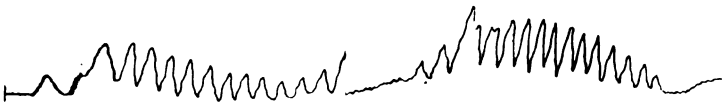


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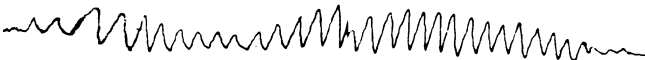


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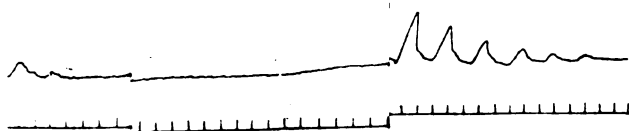
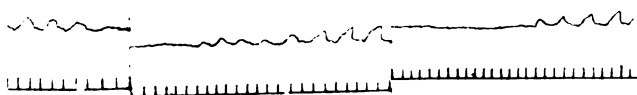
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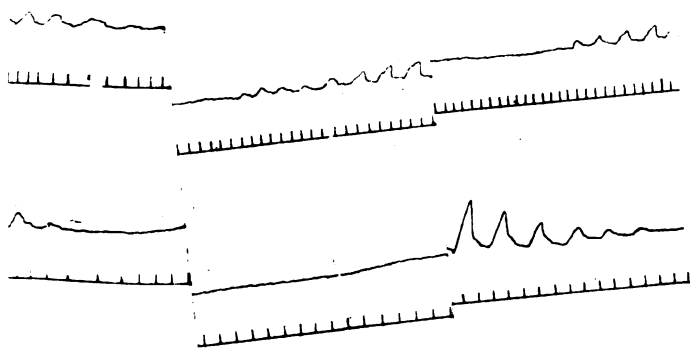
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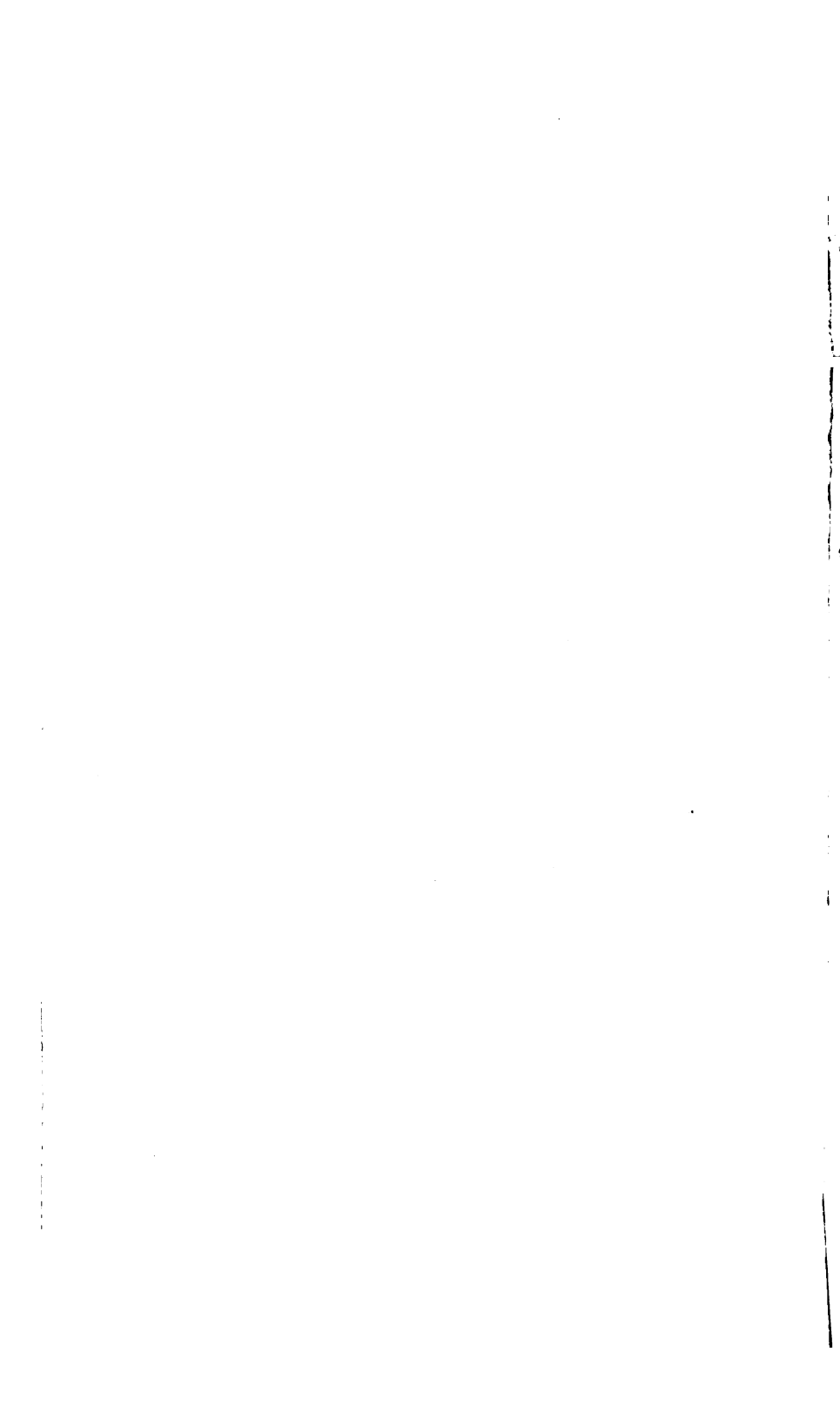
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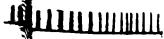
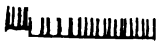
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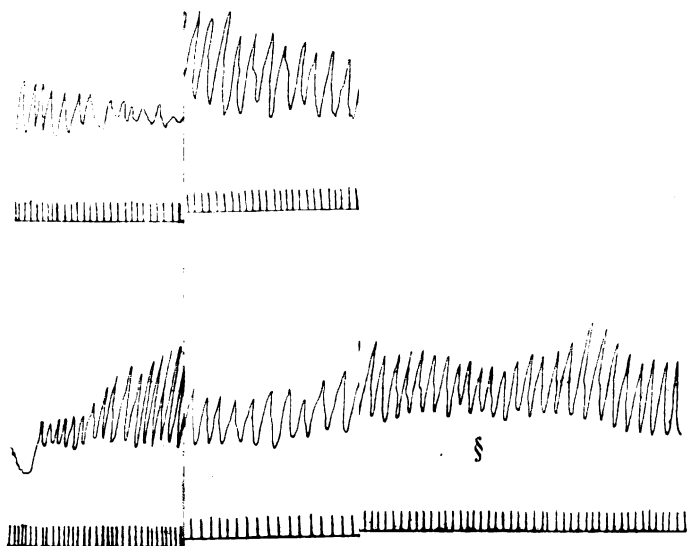


Fig. 1. Mask and valve of carbon dioxide
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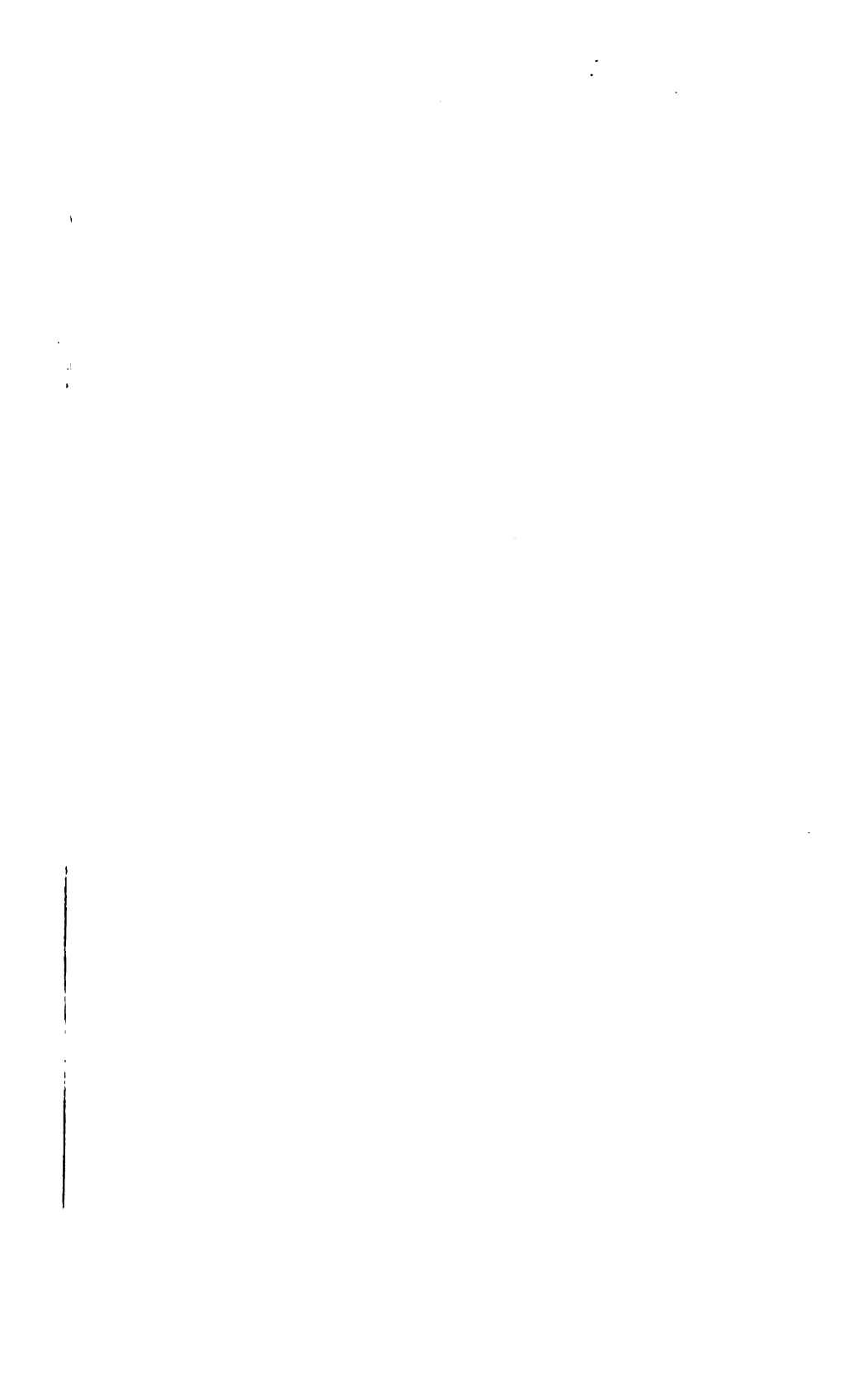
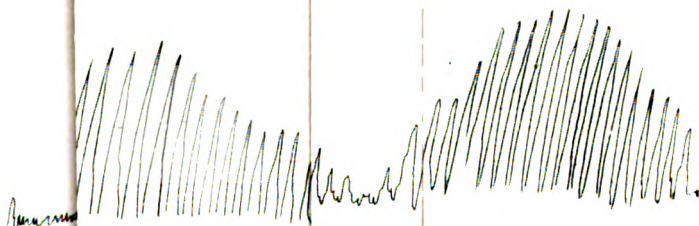
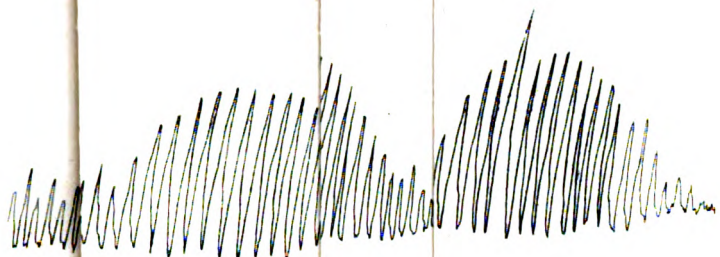
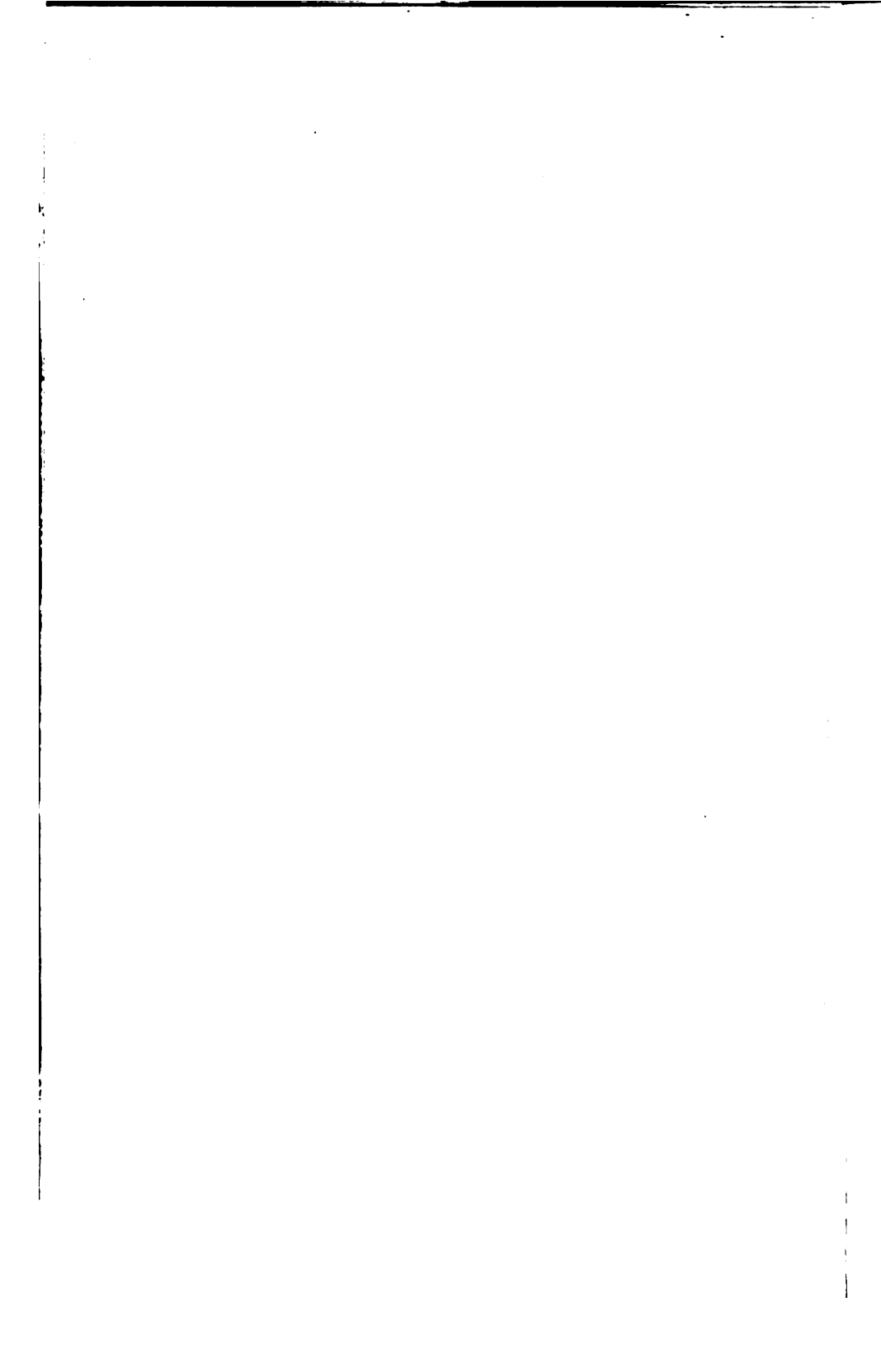
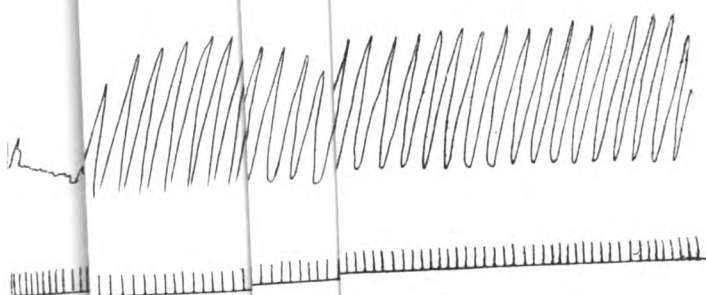
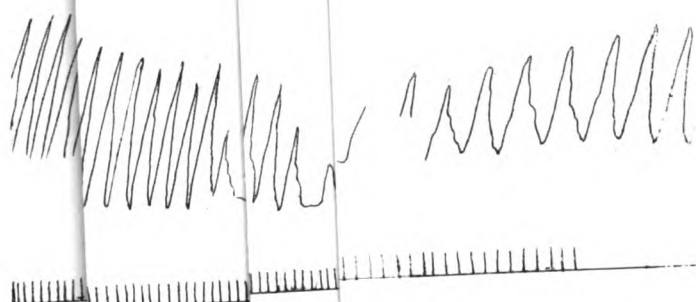
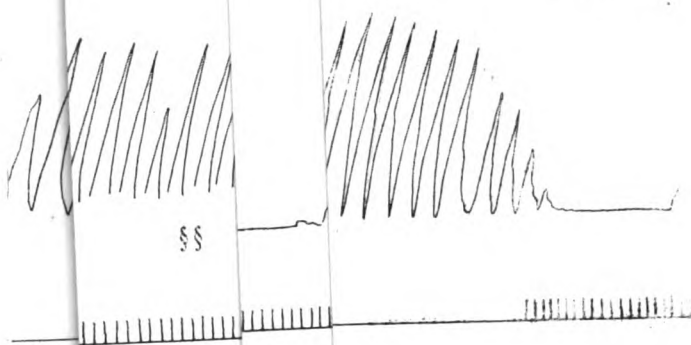


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(Read before the Royal Medical and Chirurgical Society,
January 8th, 1907.)

OBSERVATIONS UPON TWO CASES OF CHEYNE-STOKES' RESPIRATION.

By FREDERICK TAYLOR, M.D., F.R.C.P.,

M. S. PEMBREY, M.A., M.D.,

A. P. BEDDARD, M.A., M.D., F.R.C.P.,

AND

HERBERT FRENCH, M.A., M.D., F.R.C.P.

Two patients in Guy's Hospital presented the phenomena of Cheyne-Stokes' respiration in so characteristic a form that further observations were made to supplement those already recorded in the preceding paper.

CASE 1.—*Observations upon the Results of the Clinical and Post-mortem Examination.* By Frederick Taylor and Herbert French.

George J—, aged 46, a gas-work stoker, was admitted into Guy's Hospital under the care of Dr. Frederick Taylor on July 17th, 1905, and died on February 4th, 1906. During the whole of this time, six and a half months, he had typical Cheyne-Stokes' respiration, except during the three days immediately preceding death.

He had been known to have kidney disease for at least ten years, and he was admitted for an exacerbation, with

some œdema of his legs. The condition of his urine was variable. It always contained albumen, and moderate numbers of hyaline and granular tube-casts. The amount of albumen varied from a mere trace to 3 parts per thousand. The specific gravity was always low, and varied from 1006 to 1012, though on two occasions it rose to 1018. The quantity was above normal; even in the middle of August he passed as much as 92 ounces in 24 hours upon one occasion, and he frequently passed above 70 ounces.

The diagnosis was granular kidney, and this was confirmed by autopsy.

The heart was much hypertrophied, the impulse being in the fifth left intercostal space, three quarters of an inch outside the left nipple, heaving in character. There were no bruits; the first sound was prolonged at the apex, and in the aortic area the second sound was much accentuated. The pulse rate was usually between 60 and 70 per minute, and the maximum systolic blood-pressure, measured in the brachial artery by Martin's modification of the Riva Rocci apparatus, varied from 165 mm. Hg. to 178 mm. Hg. During hyperpnœa cardiac dulness could only just be detected to the right of the sternum; during apnœa this dulness increased a full inch further to the right.

The lungs were at first congested at the bases; the signs of this cleared up. Just before death there was dry pleurisy over the right lower lobe. There was no emphysema.

The gastro-intestinal viscera were natural, as were also the nerve reflexes.

There was well marked albuminuric retinitis in both eyes, with white patches of exudation, and hæmorrhages both old and recent. The patient, however, always said his eyesight was good.

The persistent Cheyne-Stokes' respiration is fully described below; it was very characteristic all the time the patient was under observation. In addition to this there

were several attacks of uræmic "asthma" during the first few days after admission. These disappeared with rest in bed, restricted proteid diet, purgatives, and digitalis.

When first admitted the man was muscular but thin. The initial œdema entirely disappeared, and relief was at first great. A month from admission the patient was able to be up and about, notwithstanding that he had Cheyne-Stokes' respiration all the time. A month later he took to his bed again, and remained there till his death. The observations upon his respiration were not begun until January, 1906, six months after he first came in.

He was always conscious, and, except for the "asthma" mentioned above, had no uræmic symptoms. He could read the newspaper with pleasure, but towards the end he took less interest in things, and when spoken to he would sometimes delay as much as half a minute before answering. This slowness of response was always more marked in apnœa than it was in hyperpnœa.

Though he took his food well he wasted markedly. His legs and body became mere skin and bone. Latterly he passed his urine and fæces into the bed, less from incontinence or unconsciousness than from simple lethargy. If a nurse were near he would ask for urinal or bed-pan; but if no nurse were near he would not be bothered.

After the first few days there was no œdema; the heart did its work well, without any of the recognised signs of failure.

Three days before death acute dry pleurisy set in, and simultaneously the Cheyne-Stokes' respiration disappeared. Death was very easy, the end coming during a deep sleep.

The autopsy showed the following organic changes:

Kidneys.—Both of the kidneys were small and granular in appearance. The capsules were adherent, the cortex thin, the arterioles prominent and thick-walled. In the right kidney there were also a series of sacculated, tuberculous abscesses. The ureters, bladder, and urethra were natural.

Heart.—The heart was much hypertrophied, more especially the left ventricle. There was no valvular disease beyond some atheroma of the aortic valves. The coronary arteries were tortuous and thick-walled, but quite pervious.

Lungs.—Small. There was recent pyogenic membrane over the right upper and lower lobes, and a recent infarct in the left lower lobe. There was no chronic lung disease.

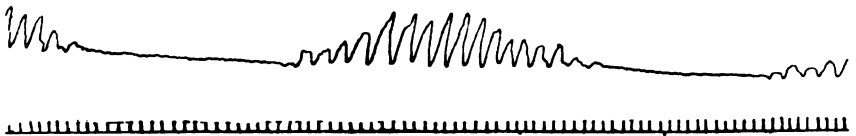
Brain.—The cerebral arteries were widely patent, thick-walled, and atheromatous. There was a small patch of softening in and around the left internal capsule. There was no hæmorrhage. The pons and medulla looked healthy to the naked eye, and were sent to Dr. Farquhar Buzzard for further examination. We are greatly indebted to him for the report given on page 42.

The remaining viscera showed no macroscopic abnormality.

Experimental Observations, especially in Relation to the Causation of Periodic Breathing. By M. S. Pembrey and Herbert French.

The patient exhibited a typical waxing and waning of the respiratory movements (Fig. 1) accompanied by a

FIG. 1.



Cheyne-Stokes' respiration. The curve reads from left to right, and the time is marked below in seconds. The small undulations during the period of apnœa are due to the beats of the heart (January 23rd, 1906).

general overflow of motor impulses; during this period he moved uneasily and complained of pain in the abdomen. During apnœa he remained conscious, but did not

speak of his own accord, and only answered questions after great delay. The duration of apnœa and breathing is shown by the tracing (Fig. 1) and the following consecutive determinations.

Date.	Apnœa.			Breathing.			
	Duration in seconds.	Rate of Pulse. Actual. Per minute.		Duration in seconds.	Rate of Pulse. Actual. Per minute.		Respira- tions.
13/1/06.	25	26	(62)	20	27	(81)	11
	22	28	(76)	20	25	(75)	10
	25	28	(67)	20	20	(60)	12
	25	25	(60)	20	33	(99)	11
13/1/06.	25	37	(89)	20	26	(78)	10
	22	32	(87)	25	27	(65)	11
	25	32	(77)	23	26	(68)	10
	22	28	(77)	21	25	(71)	10

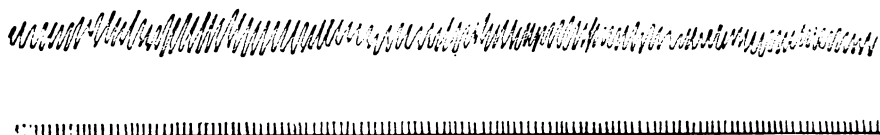
Three or four days before death (February 4th, 1906) his breathing lost the periodic type and became continuous; at this time there were signs of pleurisy, upon the right side. When the patient was asleep on January 29th his breaths were deep and regular, 30 per minute; after he awoke they were somewhat irregular, but still of the continuous type. The colour of his face was much fresher than it had been in the days when Cheyne-Stokes' respiration was present; he was, however, complaining of pain. Again on January 31st he was observed asleep; his respirations were regular and deep, and showed no periodic changes either in frequency or depth. After he awoke his respirations were still of a continuous type, but they undoubtedly showed a periodic change in depth; a series of deeper breaths followed shallower ones, and this alternation was repeated again and again. Percussion of the chest caused pain, especially upon the right side.

This disappearance of the Cheyne-Stokes' respiration is interesting; it would appear that, owing to the pleurisy, the patient was no longer able to take the very deep breaths which had characterised the height of the waxing respiration; carbon dioxide would therefore not be re-

moved so freely, and its mean partial pressure would be maintained at a higher level. It is possible that the pain caused by the pleurisy not only limited the expansion of the lungs, but also raised the excitability of the respiratory centre by impulses passing up the vagi and other nerves.

Our observations were made during the time when the Cheyne-Stokes' phenomena were at their height, and consisted chiefly in an investigation of the effects of oxygen and carbon dioxide upon the periodicity of the breathing.

FIG. 2.



The effect of pure oxygen administered by means of a mask provided with inspiratory and expiratory valves. Respiration is of the continuous type. (January 23rd, 1906.)

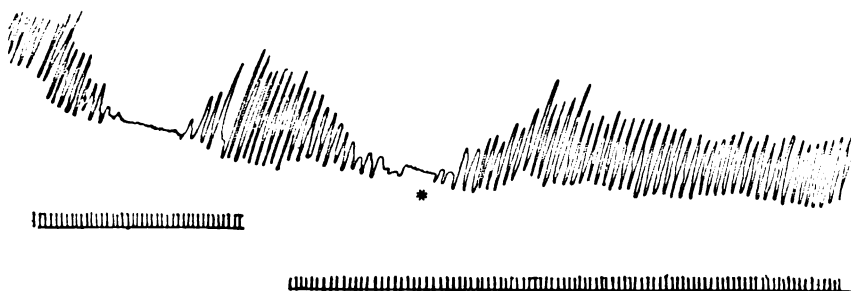
The administration of oxygen through a mask provided with inspiratory and expiratory valves caused the apnœic pause to disappear within one minute and a half. In one record, when the patient was breathing air through the mask and valves the period of breathing lasted thirty-nine seconds, and included twenty respirations; it was followed by apnœa for a period of nineteen seconds. During the breathing of pure oxygen the respirations were shallow, rapid, and continuous in type, 48 respirations in fifty-eight seconds (Fig. 2). Oxygen gave the patient much relief and removed the dusky ash-grey colour of the face.

Air containing 4·67 per cent. carbon dioxide and 20·48 per cent. oxygen was administered towards the beginning of a period of breathing; the tendency to apnœa was promptly abolished, the respirations became continuous in type, deep, and of a frequency of 48 in a minute (Fig. 3). The breathing of air containing 4 to 5 per cent. of carbon

dioxide caused the patient no distress, but several times made him cough.

Apnœa was also abolished when the patient breathed through a mask with a long rubber tube; the "dead space" was increased, and thus the inspired air, by admixture with some of the air just expired, contained a higher percentage of carbon dioxide and a lower percentage of oxygen than in normal air. Even the slight

FIG. 3.



The first portion of the tracing shows Cheyne-Stokes' respiration when the patient was breathing air through the mask and valves. At the point marked by the star a mixture of air and carbon dioxide, 20·48 per cent. oxygen and 4·67 per cent. carbon dioxide, was administered. The respirations became continuous in type. The small undulations during the period of apnœa are due to the beats of the heart. (January 23rd, 1906.)

disturbance of respiration produced by the application of the mask and valves tended at first to prolong the period of breathing and to shorten the period of apnœa, although in this case there was but a very small increase in the "dead space."

Samples of the alveolar air of the lungs were collected at different stages of the periodic breathing. The results of the analyses are given in the following table:

		Waxing Respiration.	
Date.		Carbon dioxide. Vols. per cent.	Oxygen. Vols. per cent.
13/1/06.	5th Expiration.	2·70	17·19
	"	2·01	18·01
23 1/06.	Height of Hyperpnœa.	1·87	18·51

Date.		Waning Respiration.	
		Carbon dioxide. Vols. per cent.	Oxygen. Vols. per cent.
13/1/06.	10th Expiration.	2.05	18.89
	13th ,,	1.76	19.22

There is no doubt that the true percentages of oxygen were lower and of carbon dioxide higher, for the mask did not always fit absolutely tight to the patient's bearded face. The first few respirations of the waxing respiration were, moreover, so shallow that it was difficult to obtain reliable samples, just as in the previous case.

Observations on the blood pressure of the brachial artery were made by means of Martin's modification of the Riva Rocci sphygmometer. At the height of hyperpnœa the readings for the maximum pressure were 178, 174, and 178 mm. of mercury, in the middle of the apnœic pause 178, 172, and 173, and at the end of apnœa 168, 168, and 165. Apart from the difference in blood pressure the influence of the periodic breathing was shown upon the area of cardiac dulness, which was increased by 18 mm. to the right of the sternum and 20 mm. outward to the left during the apnœic pause.

The point most to be noted is that the administration of either excess of oxygen, or of excess of carbon dioxide, in the air breathed caused disappearance of the Cheyne-Stokes' type of respiration.

The Structural Changes in the Pons and Medulla Oblongata.

Report by E. Farquhar Buzzard, M.D., F.R.C.P.

"The pons and medulla were hardened in 5 per cent. formalin, and then cut transversely into a number of thin slices. With the naked eye these slices appeared normal, except for the presence of numerous small areas of softening, some of which were of a bright red and others of a dirty yellow colour. The largest of these areas was scarcely larger than a pin's head, and they were more numerous in the medulla than in the pons. In both

regions they were more often seen in the neighbourhood of the median raphe than in the more lateral parts. A number of slices were embedded in paraffin and cut; the sections were stained either with methylene blue or with logwood and eosin.

“*Microscopical.*—Although degenerative cell changes in the various nuclei of the medulla were striking, they could only be regarded as secondary to the vascular disease which was very marked throughout the sections. In the first place, nearly every arteriole and capillary in the substance of the medulla showed general thickening, chiefly of the media, with hyaline degeneration. Some of the larger vessels, especially those near the median line, presented, in addition to the hyaline change in the media, marked periarteritis, indicated by the presence of numerous round cells in the adventitia and perivascular spaces.

“In the second place, there were many recent and some older capillary hæmorrhages, especially just beneath the floor of the fourth ventricle, in the region of the dorsal nuclei of the vagus.

“Thirdly, evidence of numerous areas of softening was to be seen in the form of fibrous scars, remains of vessels surrounded by necrotic tissue and altered blood pigment. One of these involved and destroyed a considerable part of one of the inferior olives, and others were situated more dorsally near the median raphe.

“In addition to these conditions, small vessels with hyaline walls were occasionally to be seen lying unsupported in small patches of necrosed tissue, the appearance suggesting the origin of some of the capillary hæmorrhages.

“Changes in the nuclei were chiefly of a degenerative type, the cells being shrunken, misshapen, and homogeneously stained. Chromatolytic changes were also present in some parts. The hypoglossal nucleus was less involved than any of the others. Amylaceous bodies were fairly numerous around the periphery of the medulla.”

CONCLUSIONS.

These observations upon Cheyne-Stokes' respiration confirm the results obtained in another case by Pembrey and Allen.¹ It would appear on the same grounds that the periodicity of Cheyne-Stokes' respiration is in great part due to "a diminished excitability of the nervous system associated with a defective supply of arterial blood; the carbon dioxide accumulates, and the oxygen diminishes, until at last the nerve-cells are stimulated, the waxing respirations begin and culminate in hyperpnœa, whereby a large quantity of carbon dioxide is washed out and sufficient oxygen taken in; apnœa then follows, due, apparently, to the absence of sufficient carbon dioxide to stimulate the nerve-cells.

"The inhalation of air containing more than 2 per cent. of carbon dioxide abolishes apnœa, by maintaining the partial pressure of the carbon dioxide in the alveolar air and blood at its stimulating valve.

"The administration of pure oxygen by means of a mask and valves abolishes apnœa by maintaining the partial pressure of carbon dioxide in the blood at its stimulating valve. The respiratory centre is no longer excited by lack of oxygen to send out the forcible impulses which had previously resulted in excessive ventilation of the lungs, whereby carbon dioxide had been washed out of the alveoli and blood."

CASE 2. F. H.— Observations by M. S. Pembrey and A. P. Beddard.

F. H—, aged 45, was standing in a lift on January 3rd, 1906, when the wire cable broke, and he fell in the lift a distance of forty feet. Both his thighs and the fingers of his left hand were broken, but his head was apparently uninjured, and he was able to crawl out of the lift.

On admission to the Hospital he was in a dazed con-

¹ See the preceding paper.

dition, but was able to answer questions sensibly. Thirty-six hours after the accident he slowly passed into a delirious condition. His respirations were rapid, about 40 per minute, his pulse about 120, his temperature varying, but never rising above 100°. He then gradually became comatose, and, after remaining in this condition for two or three days, improved, and by January 9th was sensible at times, but often very restless, stupid, and semi-conscious. His mental condition slowly improved, and by January 13th was apparently normal.

The exact date of the onset of the Cheyne-Stokes' respiration is uncertain, but on January 12th it was well marked. Examination then showed no abnormality in the heart and lungs, no signs of fractured skull, no paralysis; his pulse was of good tension and regular; his urine was normal; his breathing was of the Cheyne-Stokes' type; a period of waxing and waning respirations was followed by a period of apnœa. During apnœa he either closes his eyes, as if he were asleep, or shows conjugate deviation of the head and eyes to the right, the eyes remaining open. He makes no attempt to answer questions. During the period of breathing he rapidly wakes up and makes a series of forcible movements, which are nearly constant in form at the corresponding stages of succeeding periods of breathing; this repetition is especially seen in the movements of the right arm and head, and the movement of the right hand over the top of the head. He slowly answers questions during this time. The following figures give the duration in seconds of several periods of apnœa and breathing.

Date.		Apnœa.		Breathing.
12/1/06.	...	15	...	25
		15	...	
		10	...	25
		15	...	25
18/1/06.	...	25	...	17
		17	...	21

The number of respirations in the periods of breathing varied from 10 to 20 at different times, and were not easily recorded owing to the movements of the right arm and head.

The following figures give the duration in seconds of consecutive periods of apnœa and hyperpnœa, when the patient was breathing air through a mask and valves.

Date.	Apnœa.	Breathing.	Apnœa.	Breathing.
18/1/06.	12	26	→ 22	27
	16	22	8	123
	18	23	21	21
	20			

Pure oxygen was then given; the respiration in ten minutes became continuous, the rate of breathing being 14 per minute. Breathing through a mask and long tube abolished apnœa, and any disturbance of the patient tended to shorten the apnœic period.

Samples of the alveolar air of the lungs were collected, but they were obtained with difficulty owing to the forcible movements which, as already described, always occurred during the period of breathing. The patient, moreover, had a thick beard, which rendered difficult the adaptation of the mask in an air-tight manner.

Date.		Waxing Respiration.	
		Carbon dioxide. Vols. per cent.	Oxygen. Vols. per cent.
13/1/06.	2nd Expiration.	3·82	15·03.
	3rd "	3·97	15·75.
	4th "	4·13	15·75.
12/1/06.	5th "	2·63	17·99.

Samples taken on January 17th, when the patient's breathing was of the continuous type, gave results:—Carbon dioxide 3·60 and 4·29, oxygen 16·88 and 15·77 vols. per cent.

The Cheyne-Stokes' respiration was more marked during sleep; it disappeared on January 22nd, but as late as

February 18th it recurred from time to time in a well marked form, especially during sleep and after the patient had complained of a bad headache.

The blood-pressure in the brachial artery was determined on January 13th by Martin's modification of the Riva Rocci sphygmometer; for apnœa the readings were 152, 146, and 142 mm. of mercury, for the period of breathing 160 mm. It must be remembered that the latter period was accompanied by forcible movements of the arm and upper part of the body.

The exact lesion of the brain in this case is uncertain. There was no wound on the scalp, no evidence of fractured skull, and no sign of hæmorrhage on the surface of the brain. It seems likely that the cortex of the brain was bruised, and that the symptoms of cerebral irritation and compression were due to that cause. From the nature of the forced movements, it would seem likely that the frontal lobes had been contused. The question arises whether this cerebral injury had any connection with the Cheyne-Stokes' respiration, and if so, what was the nature of that connection. The symptoms of cerebral compression had passed off before the Cheyne-Stokes' respiration ceased, and this fact makes it unlikely that a gross change in the cerebral circulation was the cause of the periodic breathing. On the other hand, there is the possibility that the cerebral respiratory centre located by various observers in the cortex of the frontal lobe may have been injured, and thus brought about the periodic modifications in the excitability of the bulbar centre.

During the time of observation the patient received no drugs, such as chloral and morphia, to the action of which the periodic breathing might be attributed.

The patient, who was under the care of Mr. Lane, made a satisfactory recovery.

CONCLUSION.

In this case the condition of the nervous system could not be determined, and direct evidence of a defective

supply of arterial blood was wanting. The administration of pure oxygen abolished apnœa, but not so readily as in the two other cases recorded.

A preliminary account of these cases was communicated to the Physiological Society on February 24th, 1906 ("Proc. Physiol. Soc.," 'Journ. Physiol.,' vol. xxxiv, 1906).

The expenses of the investigation were defrayed from a grant from the Royal Society.

Our thanks are due to Mr. Lane for the facilities we received of observing the patient under his care.

ASPIRATION OF A PNEUMOTHORAX UNDER THE X-RAYS.

By JOHN FAWCETT, M.D.

THE following case of pneumothorax is of interest in that it is, as far as I am aware, the first of its kind to be recorded as treated by aspiration, the patient's thorax, during the process, being under observation by means of the X-rays. From the time of onset of the pneumothorax until the patient's discharge from the hospital an interval of a month elapsed; for the first two and a half weeks of that period the patient was kept in bed, and showed little evidence of improvement as regards the absorption of air from the pleura and of expansion of the lung. The improvement and relief produced by aspiration were immediate.

Inasmuch as all that is taking place in the chest and lung can be seen during aspiration by this method, the advantage of it is obvious. Instead, too, of a lung permanently damaged from compression by air, or a long-drawn-out illness, the air can be withdrawn and immediate relief afforded to the patient, provided the opening in the lung is closed at the time of aspiration. If the hole in the lung is not closed, then the lung will not be seen to expand when aspiration is commenced, and the aspiration can at once be stopped. As far as I can see, provided all precautions are taken, nothing but good can result from this treatment in suitable cases. I am much indebted to

Mr. E. W. H. Shenton for the X-ray photographs, and, for the report of the case, to my "clinical," Mr. C. H. Rippmann.

William G. S., æt. 22 years, was admitted into John Ward, under my care, on June 5th, 1907, with a pneumothorax of the right side.

Previous history.—The patient said that he had been a strong man until an attack of "pneumonia" two years previously, since which time he had not felt so well. He works in the Millwall Dock. He had not lost weight, nor had he had any cough, expectoration, or hæmoptysis.

History of present illness.—The patient first felt pain, in the right side, on the evening of June 3rd; after this the pain was less until the evening of June 5th, when it became more acute again. At the time when the patient first felt the pain in his side he was sitting quietly, drinking, in a public-house. He has no recollection whatever of exerting himself in any way previous to the onset of the pain.

Condition on admission.—Temperature 102°, pulse 128, and respiration 32 per minute. The patient was somewhat dyspnoeic, and there were the usual typical physical signs of a pneumothorax on the right side. The heart's impulse was felt with difficulty just external to the left nipple line.

There was no evidence of any effusion of fluid into the right pleural cavity, the note being hyper-resonant down to the extreme base.

Progress of case.—The temperature remained raised for a week, as may be seen on reference to the chart; it then fell to normal, and remained so until the patient was discharged.

June 10th. The patient's chest was skiagraphed. The dark oval shadow of the compressed right lung was very clearly seen on the screen, the remainder of the right pleural cavity being more translucent than was the left side. On respiration very little, if any, expansion of the right lung occurred. A photograph was taken, which is reproduced in Fig. 1.

June 15th. A very feeble and distant respiratory murmur could be heard over the upper part of the right lung; otherwise there was no change in the patient's condition.

Aspiration of a Pneumothorax under the X-rays.

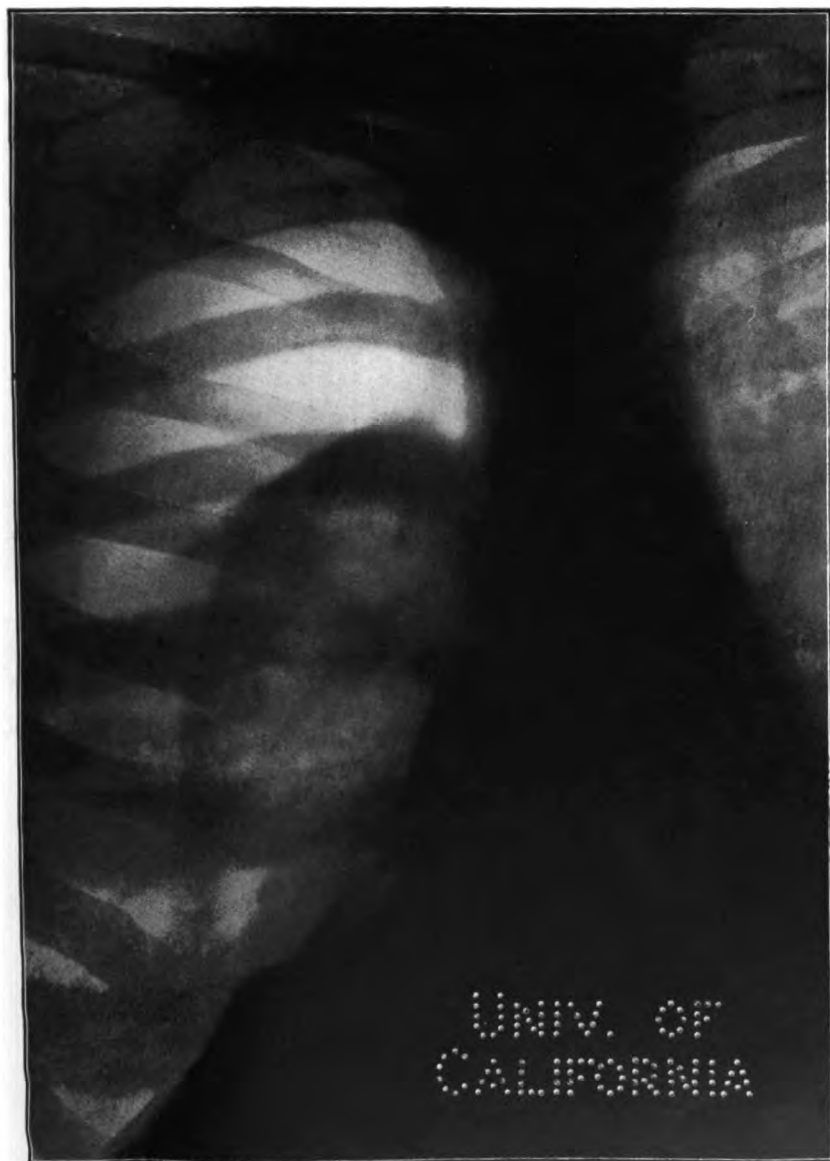
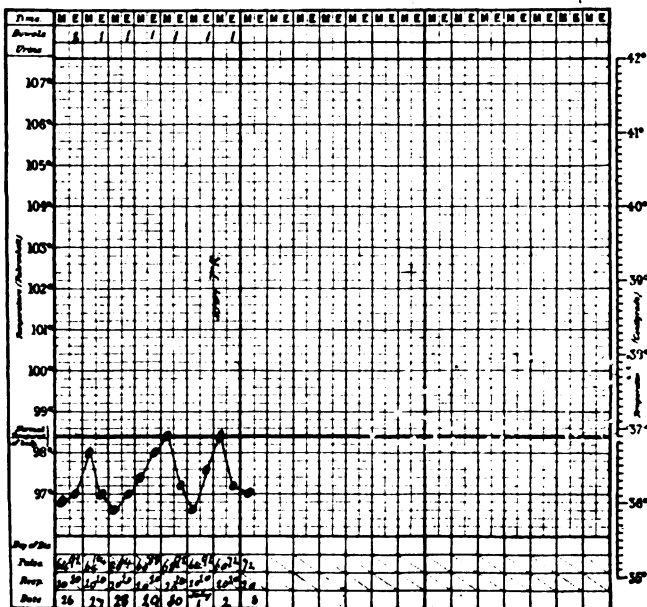
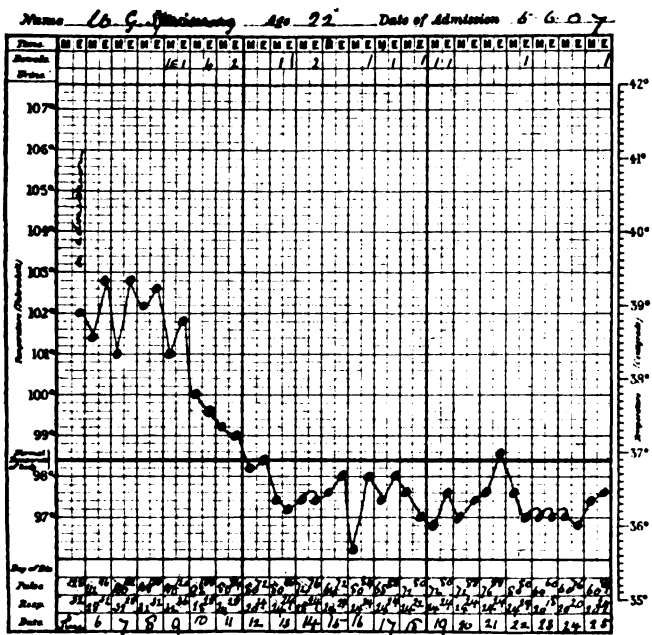


Fig. 1.

Pneumothorax, showing the shadow of the compressed lung before the air was aspirated from the pleural cavity.

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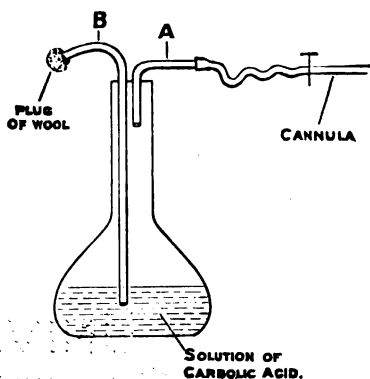


June 17th. No change found in the position of the lung on examination with the X-rays.

June 21st. The "bell sound," which was everywhere audible on admission, was less marked, and the respiratory murmur over the upper part of the lung was, perhaps, a little better heard, but it was still very faint and deficient. On examination with the X-rays the lung was seen to have expanded slightly.

It was now nineteen days since the onset of the pain, and the temperature had been normal for ten days. As very little expansion of the compressed lung had taken place it was decided to try and remove the air from the pleura, and so allow the lung to expand again. The procedure adopted was as follows:—

The patient was placed on his back on the couch in the X-ray room. The screen was then placed on the front of the chest, and a trocar and cannula, of the form commonly employed in aspirating the pleural cavity, was then inserted into the right pleural sac immediately in front of the posterior axillary fold in the 6th or 7th space. The trocar being withdrawn, the cannula was then connected up with a sterilised flask containing a solution of carbolic acid (1-40).



The cannula was connected with the tube A: on turning the tap of the cannula and so placing the pleural cavity in communication with the flask, air was seen to bubble through the tube B at each inspiration: this showed that the air in the pleural cavity was under negative pressure during inspiration.

Year of
Celebration

Aspiration of a Pneumothorax under the X-rays.

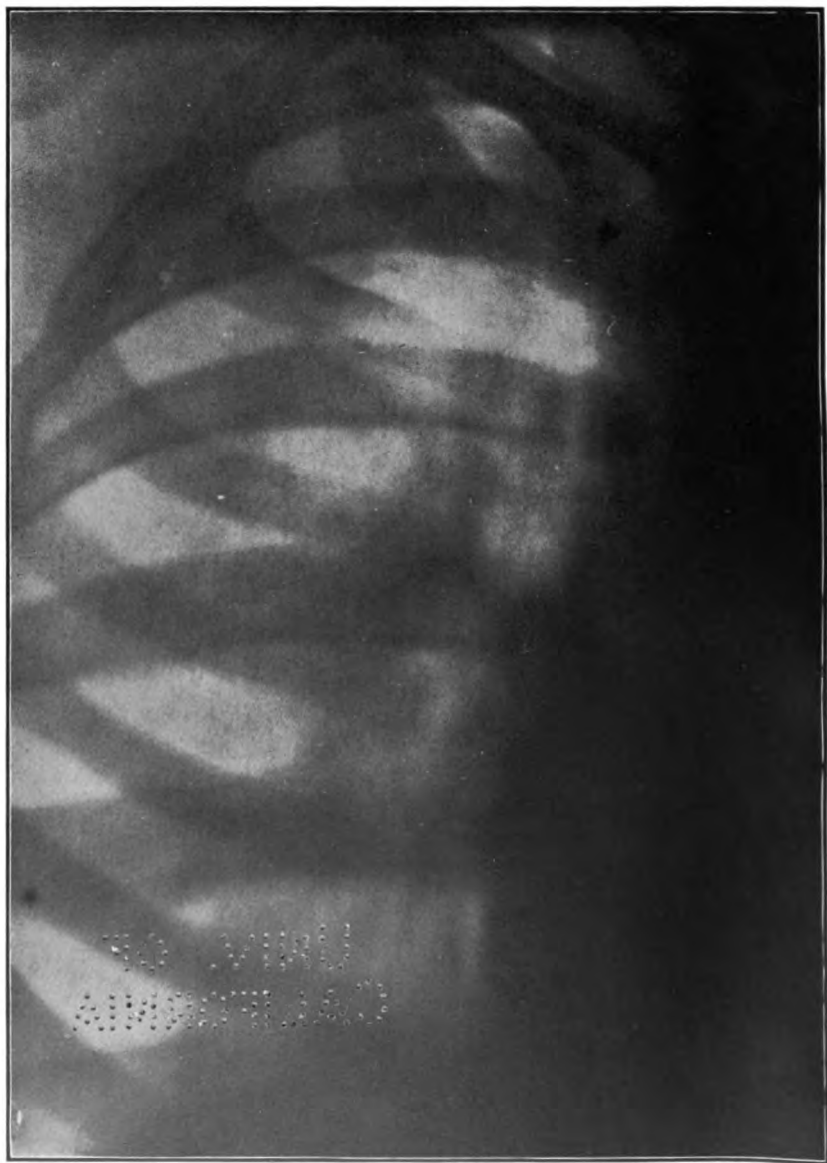


Fig. 2.

Photograph taken immediately after aspiration. The lung is expanded and occupies the normal position.

The tap of the cannula was then turned off, and the tubing attached to the cannula was fixed on to a sterilised Winchester-quart bottle from which the air had been partially exhausted. On putting the cannula into connection with this bottle, by turning the tap, the lung was at once seen on the X-ray screen to expand, and the air could be felt passing through the tubing from the pleural sac into the Winchester-quart bottle. As the lung expanded more and more, the cannula was gradually withdrawn until it was flush with the chest-wall, and when the lung was fully expanded the cannula was withdrawn and a dressing placed over the puncture wound.

The patient was kept on the X-ray couch for a short while longer; the right lung was seen to remain expanded, and to expand and retract with the respiratory movements, the diaphragm of the right side now moving freely, although perhaps a little less so than on the left side. Fig. 2 is a reproduction of the skiagram which was taken on this day.

The patient was carried back to bed as, although the hole in the lung was closed, we did not wish to run any risk of rupturing the lung again by an excessive movement.

The advantage gained by aspiration under the X-rays was that we were able to see what was going on in the damaged lung. If we had found that, when the pleural cavity was connected up with the partially-exhausted Winchester-quart bottle, the lung did not expand, then we should at once have stopped aspirating. As it was, however, the lung was seen to expand directly the connection was made, and to remain expanded, and so it was clear that the opening in the lung was closed, and that gentle suction of the air from the pleura had not opened it again.

June 22nd. Examination with the X-rays showed that the right lung was still expanded very well, and indeed there was little, if any, difference to be noticed on comparing the movements of the two lungs.

June 25th. Re-examination with X-rays showed that the lung was acting perfectly. Although this was the case, yet the

base of the right lung was not so resonant to percussion as the left, and the respiratory murmur was distinctly less audible on this side and remained so up till the time of patient's discharge.

In the absence of the evidence obtained by means of the X-rays, which showed that the right lung was expanding well, I should have said that the physical signs indicated a deficient expansion. The patient's after-progress was quite satisfactory, and he was sent to a convalescent home on July 3rd. He was allowed to get up two days after the operation.

Ætiology.—The cause of the pneumothorax remained unexplained. We were unable to find any evidence of tubercle in the lungs, or of any other lesion. The tuberculo-opsonic index was kindly determined by Dr. Eyre on four occasions, and it was practically normal, as the following figures show :—

June 15th	0.96
„ 22nd	0.95
„ 26th	0.8
July 1st	1.0

MICROCOCCUS MELITENSIS AND ANTISERUM.

(Report to the Mediterranean Fever Commission,
June and October, 1906.)

By J. W. H. EYRE, M.D.

THE first serious attempt to produce an antiserum for therapeutic use in Malta Fever was made by Wright, who, in 1895, treated goats and in the following year a horse by the subcutaneous injection of "killed" cultures of *Micrococcus melitensis*. The serum obtained from the goats appeared to possess but little agglutinative power, and when employed in the treatment of monkeys, either previously or subsequently to the injection of living cultures of the *Micrococcus*, exhibited neither protective nor curative properties. The serum of the horse was further used in the treatment of patients suffering from Malta Fever, and some of these human cases recorded by Aldridge¹ in 1898 showed, subsequently to the administration of the serum, improvement which was ascribed to the action of the serum. No further observations or experiments in this direction have, however, been recorded since. In 1903 I commenced a series of experiments dealing with the immunisation of rabbits and of guinea-pigs, in the hope of obtaining a bactericidal serum of demonstrable potency; next goats were tried, and finally, in 1905, I undertook the treatment of a horse. The results

¹ 'Lancet,' vol. 1, 1898, p. 1394.

obtained to date are by no means so encouraging as was anticipated, but certain points have been established which help to elucidate phenomena observed during the course of experimental work on the *Micrococcus*, to which points it appears advisable to draw attention.

My early experiments, in which the rabbit as well as the guinea-pig was employed, confirmed Durham's² valuable observations; his results may be summarised as follows, the illustrative cases being taken from my own note-book:—

(a) That the development of specific agglutinins in the blood was slower in rate and less in amount in the most severe and in the least severe infections (compare Animals Nos. 1 and 2 Table I). Speaking generally, the formation of large quantities of agglutinins took place when the resisting power of the infected animals was considerably but not *over* strained.

(b) That there was apparently little direct relationship between agglutinins and antitoxic or antibacterial substances, as the blood of infected animals frequently showed a high agglutinative power for some time prior to a fatal termination (see Animals Nos. 3, 4, and 5, Table I).

(c) And, finally, that animals whose blood at death possessed a low agglutination index often showed a general blood infection with abundant cocci, whilst it was frequently observed in those with high agglutinative power that cocci were either absent from the blood of the general circulation or present in very small numbers (compare Animals Nos. 1 and 3, Table I).

Occasionally, however, the cocci are present in the peripheral blood in enormous numbers, even when the sedimentation value of the serum is fairly high (see Animals Nos. 4 and 5, Table I).

In addition it was found that the intravenous injection of graduated doses of killed cultivations of *Micrococcus melitensis* provoked the formation of agglutinins (though, speaking in general terms, in lesser quantities than followed the injection of suitable doses of living cultures), and that after agglutinins had been formed in demonstrable quantities, the immediate effect of the introduction of a further dose of killed culture was to

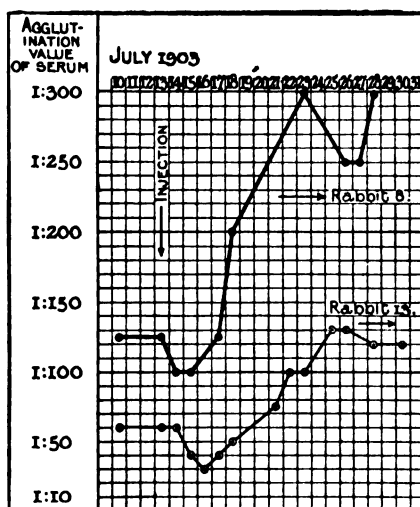
² 'Journ. of Path. and Bact.,' vol. 5, 1899, p. 377.

TABLE I.

Reference No.	Guinea-pig No.	Dose of living culture.	Method of inoculation.	Sedimentation value of serum.	Interval between inoculation and death.	Number of cocci per 10 cm. heart blood at death.
1	63	loop.	Intracerebral	1 : 10—	10 hours	6000
2	12B	0.001		1 : 500+	28 days	Nil
3	15	1		1 : 1100+	27 hours	3
4	90	1		1 : 600+	4 days	500
5	19c	1		1 : 1000+	21 "	1000

temporarily diminish the quantity of agglutinins present in the serum, and its more remote effect to provoke a marked increase (see Chart I). Again, it was often observed that if the injections were too frequently repeated, this immediate diminution was cumulative (see Chart II), conclusively showing that the formation of agglutinating substances for *Micrococcus melitensis* followed the same laws as those of typhoid, dysentery, and other better-known agglutinins.

CHART I.



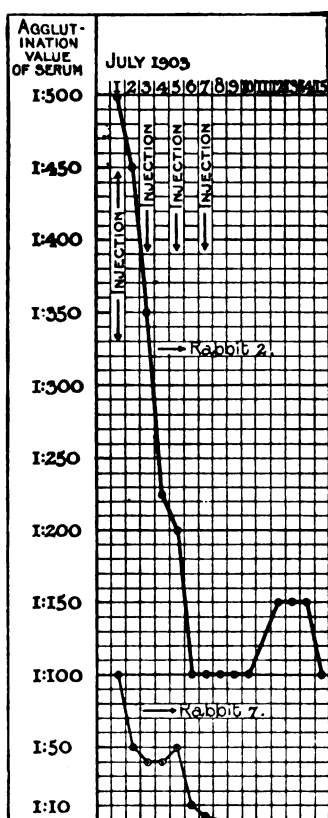
Showing the immediate and remote effects upon the sedimentation index of the experimental rabbit produced by the intravenous administration of 2 milligrammes of "killed" cultivation of *Micrococcus melitensis*.

After the long-continued treatment of the rabbit by repeatedly injecting suitable doses of killed cultures, and the establishment and maintenance of a high agglutinative power in the blood, the introduction of even comparatively small amounts of living virulent cultures almost invariably caused the death of the animal, whilst the highly agglutinating blood serum of the treated animals failed to protect normal rabbits against infection or modify the effects of such infection.

E.g., Rabbit No. 8, weighed 3,000 grammes, under treatment for seven months, litre of serum=1 : 1,500, received one loop of a three-day old agar culture of *Micrococcus melitensis* intracerebrally. Death occurred in ten days from *Micrococcus melitensis* septicæmia, and *post-mortem* all the organs and tissues were found to be crowded with the micrococci.

The difficulties in the way of obtaining serum in sufficient quantity from the rabbit for extensive tests of its influence on the course of infections resulting from the injections of other animals with *Micrococcus melitensis* led me to attempt the immunisation of goats, employing at first the method of intravenous injection of killed cultures of *Micrococcus melitensis*. After five months' work it was found that the agglutinative power of the blood serum could not be pushed much beyond 1 : 200, although the amount of inoculum introduced at the latter injections was equivalent to the entire bacterial growth of one Roux culture bottle. The subsequent injection intravenously of living cultures elicited no adequate response, although it yielded the further information that the coccus remained alive in the general circulation and could be recovered from the peripheral blood of the animal at least a month after injection. On the other hand, owing to the low virulence of the culture of *Micrococcus melitensis* with which I was working, the course of the infection in the experimental animals extended to months, and it became impossible to ascribe therapeutic value to the goat's serum when an animal treated therewith survived the control by two or even three months—even when at the *post-mortem* examination cocci were absent from the organs, bone marrow, and urine; for similar findings were not infrequently recorded in the control guinea-pigs.

CHART II.



Showing the effects produced upon the sedimentation index of the experimental rabbit by the repeated injection of small doses (0·001 of a loop) of living cultivations of *Micrococcus melitensis*.

Note.—Rabbit No. 2 died July 30. *Micrococcus melitensis* recovered in large numbers from all organs.

Rabbit No. 7 died August 28. *Micrococcus melitensis* not recovered.

Under these circumstances I directed my attention to the exaltation of the virulence of the *Micrococcus melitensis* for the guinea-pig, with the result (as detailed in a previous paper in the Reports to the Mediterranean Fever Commission—Part II, p. 67) that the contents of a loop holding some 0·5 milligramme of culture could be depended upon to produce death within seven

days. Such a dose, although obviously not the minimal fatal dose, is referred to as the "standard" dose.

A chestnut mare was purchased by the Commission at the end of March, 1905, and after satisfactorily passing the tuberculin and mallein tests its serum was tested against an emulsion of *Micrococcus melitensis*, and was found to be totally devoid of agglutinative power on the coccus, even when equal quantities of the serum and emulsion (1 : 2) were placed in contact. Treatment was begun on April 3rd by the subcutaneous injection of 10 milligrammes of *Micrococcus melitensis* culture, previously suspended in 10 c.c. of saline solution and killed by heating to 59° C. for 30 minutes in water bath. In this connection I may mention that the strain of *Micrococcus melitensis* used throughout these horse injections was the one, highly virulent for guinea-pigs, mentioned above.

At intervals of about one week, the exact time being determined by attention to such points as the general condition of the mare, temperature, etc., the injection was repeated and the size of the dose of killed culture gradually increased until after nearly two months' treatment it had reached 250 milligrammes. The quantity of agglutinins formed in response to these injections was, however, small, and a complete reaction could not be obtained in higher dilutions than 1 : 5. The seat of inoculation was then changed, and 18 milligrammes of dead cocci injected directly into the external jugular vein, with the result that the agglutinins immediately increased in amount and the sedimentation curve rose to 1 : 100. Living cocci from three-day old agar cultivations were then substituted for the "killed" cultures, and were injected intravenously (gradually increasing doses from 5 milligrammes up to about 3,000 milligrammes being introduced on 10 separate occasions during the following six and a half months), and in this series the interval between the injections was regulated by the movements of the sedimentation curve, which invariably responded to an injection in the manner already referred to and graphically represented in Chart I. The details of the 18 injections are summarised in the accompanying table (II).

TABLE II.—Details of Horse Inoculations.

No. of inoculation.	Date.	Character of inoculum.	Approximate size of dose of cocci.	Bulk of emulsion injected.	Site of inoculation.	Resulting sedimentation value of serum.
1	3/4/05	" Killed " cultivation	mg. 10	c.c. 10	Subcutaneously	1 : 2—
2	10/4/05	"	25	10	"	1 : 2—
3	15/4/05	"	25	10	"	1 : 2—
4	25/4/05	"	50	20	"	1 : 2—
5	1/5/05	"	100	50	"	1 : 2—
6	11/5/05	"	100	50	"	1 : 2—
7	20/5/05	"	250	50	"	1 : 5+
8	2/6/05	"	18	10	Intravenously	1 : 100+
9	15/6/05	Living cultures	5	20	Intravenously	1 : 600+
10	26/6/05	"	5	10	"	1 : 1500+
11	4/7/05	"	10	25	"	1 : 2000+
12	13/7/05	"	25	50	"	1 : 1000+
13	29/7/05	"	25	50	"	1 : 5000+
14	10/8/05	"	50	50	"	1 : 5000+
15	23/8/05	"	50	50	"	1 : 2000+
16	26/9/05	"	1250	50	"	1 : 2000±
17	12/10/05	"	1250	50	"	1 : 1500+
18	9/12/05	"	3000	100	"	1 : 3000+

The clinical phenomena exhibited by the animal subsequently to an injection were remarkably few. The temperature invariably rose within a few hours of the injection, but rarely more than 1°·5 to 2° C., and the mare was " off her feed " for perhaps 24 to 36 hours. The temperature rapidly fell, and was again normal within two or three days. After a subcutaneous inoculation of the dead bodies of the cocci a small local swelling appeared in about 12 to 18 hours, which was tender and " boggy " to the touch. This was soon absorbed as a rule, but on one occasion it persisted for some days, became conical in shape, and the apex of the cone became so soft as to induce me to incise at this point. No pus, however, was present: cultures from the œdematous subcutaneous tissue remained sterile, and the wound rapidly healed. On another occasion the emulsion of living cocci was prepared with sterile distilled water instead of normal saline solution and injected intravenously, with the result that a certain

amount of thickening occurred along the course of the external jugular vein, requiring nearly a week for its complete absorption, and causing a heavy fall in the sedimentation value of the serum. Beyond these two mishaps nothing occurred to disturb the progress of treatment, and in February, 1906, some six weeks after the final bleeding, the mare had immensely improved in weight, general appearance, and spirit since her purchase by the Commission.

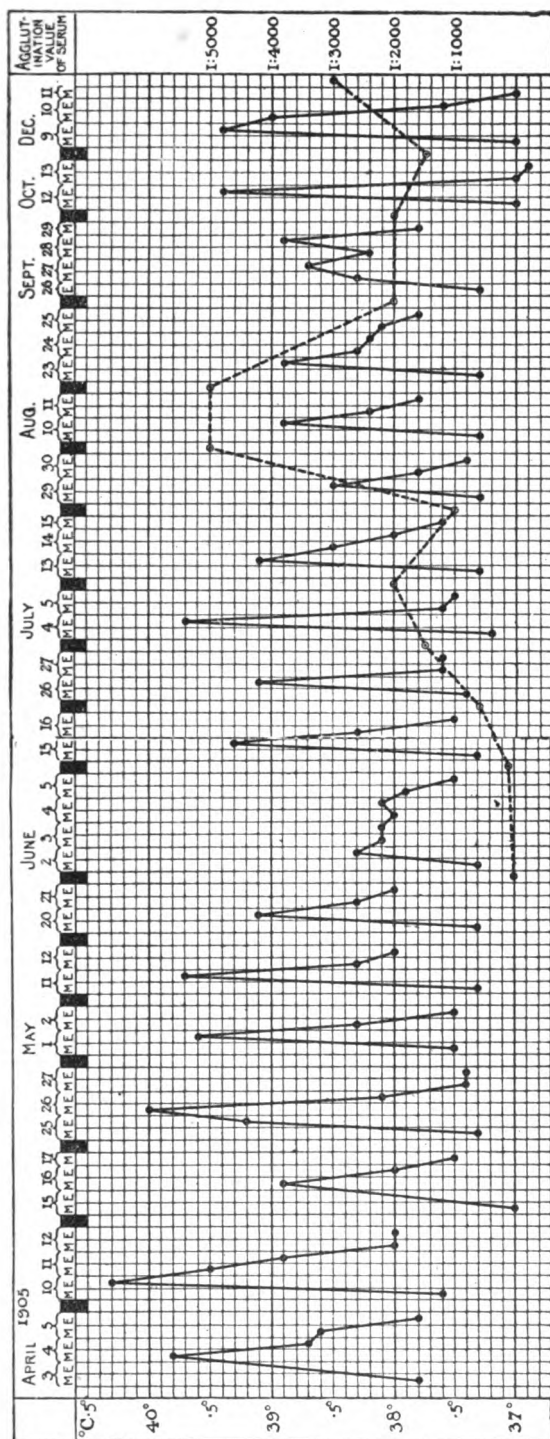
In the accompanying chart I have abstracted the movements of the curves of the temperature, and of the sedimentation value of the serum, corresponding to each individual inoculation.

In addition to the samples of blood frequently abstracted to determine the amount of agglutinins present, larger quantities (some 250 c.c.) were drawn at intervals, and on the separation of the serum, tests were made in the first place of its sterility and in the second of its protective properties. With reference to the first point, so far as could be determined by plate and tube cultivations, the serum, when carefully decanted from the blood clot, was absolutely sterile, but the injection of animals showed that a sufficient number of micrococci were present in the blood serum when this had been drawn within about three weeks of an inoculation to cause a fairly acute infection, but that by the end of about four weeks after injection, the horse had been able to remove all living cocci from the general circulation, and the serum was then innocuous and presumably sterile.

These results are summarised in Table III.

The question of protective properties may be easily dismissed. In no case (and some 20 guinea-pigs were employed for the experiments with the serum obtained at the last bleeding in February, 1906) did the subcutaneous injection of even large quantities of the serum, 10 c.c. and 20 c.c., prevent the subsequent infection of the experimental animal by a "standard" dose of *Micrococcus melitensis* injected intracerebrally, or do more than slightly retard the fatal termination. When, however, 0.1 c.c. of serum and a "standard" dose of Micrococci were simultaneously introduced into the cerebral tissue the animal remained unaffected.

CHART III.



Showing the response of the temperature (continuous line) and sedimentation (interrupted line) curves of the Malta Fever mare to each of the 18 injections. The average temperature of the normal horse is 37°-57 C. (Sims Woodhead, "Proc. Physiological Soc." vol. 23, 1899, pp. 15-18.)

TABLE III.

Date.	Animal and number.	Injected with horse serum.		Method of inoculation.	Result.
		Quantity.	Obtained—days since last injection.		
23/8/05	Guinea-pig 16	c.c. 10	13	Subcutaneously	Death in 3 days, <i>M. melitensis</i> recovered.
"	" 57	10	13	"	Death in 2 days, <i>M. melitensis</i> recovered.
15/9/05	" 64	10	21	"	Death in 3 days, <i>M. melitensis</i> recovered.
22/9/05	" 16A	10	28	"	Animal unaffected—serum absorbed.
24/11/05	" 17	10	28	"	Animal unaffected—serum absorbed.
"	Rabbit 171 ...	10	28	Intravenously	Animal unaffected.

Note.—It was probably during the dilution of the serum drawn on August 20th in readiness for me to determine its sedimentation value, or during the performance of the *post-mortem* on guinea-pigs Nos. 16 and 57, that my colleague, Dr. Price Jones, became infected, and 15–17 days later developed a typical attack of Malta Fever.

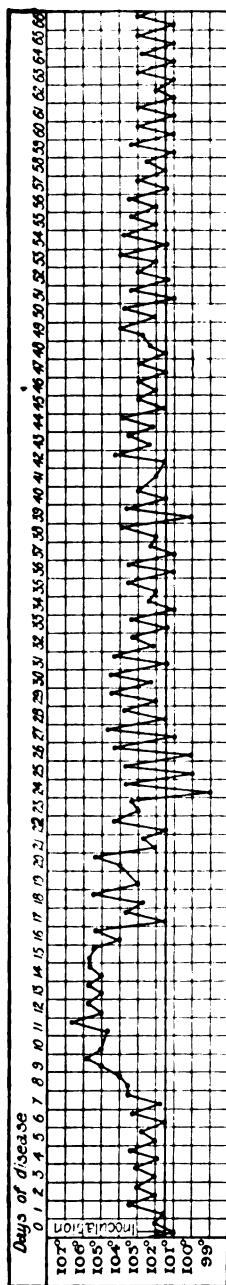
TABLE IV.

Guinea-pig No.	Dose of culture.	Method of inoculation.	Dose of Serum.	Method of Injection.	Result.
140	loops. 1	Intracerebrally	c.c. 5	Subcutaneously	Death in 6 days, <i>M. melitensis</i> recovered.
141	2		5	"	Death in 36 hrs., <i>M. melitensis</i> recovered.
142	1		0.1	Intracerebrally	Unaffected.
143	1		—	—	Death in 36 hrs., <i>M. melitensis</i> recovered.

The possible possession of therapeutic properties by this serum was next investigated experimentally upon the monkey.

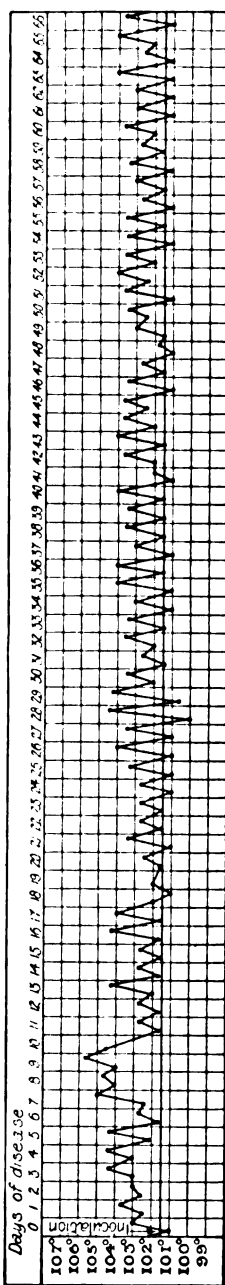
Six healthy monkeys (*Macacus rhesus*), numbered 1 to 6 inclusive, were selected, and each injected subcutaneously with 0.1 of a loopful of cultivation of *Micrococcus melitensis* (grown for 24 hours at 37° C. on an agar slope), emulsified in 1 c.c. normal saline solution. Eight days later, when signs of successful infection—rise of temperature, appearance of agglutinins in blood, etc.—were apparent, Nos. 1 and 2 were set aside for observation as controls; Nos. 3, 4, and 5 received 3 c.c. horse serum subcutaneously daily for eight days, and No. 6 received 3 c.c. horse serum injected directly into the external saphenous vein daily for a similar period. The result was by no means encouraging, and is well shown in the accompanying series of charts, for while Monkey No. 4 showed a comparatively even temperature and an absence of marked pyrexia that might be attributed to the action of the serum, the charts of the remaining three serum-treated monkeys show no marked differences, so far as concerns the range and duration of pyrexia, from those of the two controls, while throughout the course of the experiment simple visual observation of the infected animals was insufficient to enable one to distinguish between the controls and those treated with serum.

The serum was also used in the treatment of one case in man, but beyond steadying the pulse and bringing it down from 108 to 96 per minute, a result which might equally well have been achieved by a simple injection of normal saline solution, no further effect could be detected.

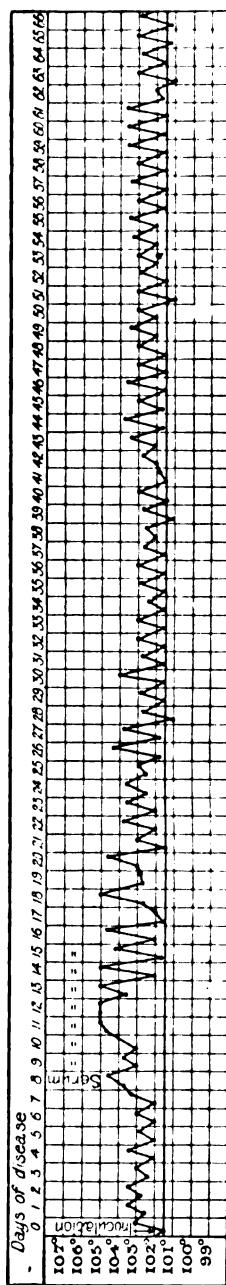


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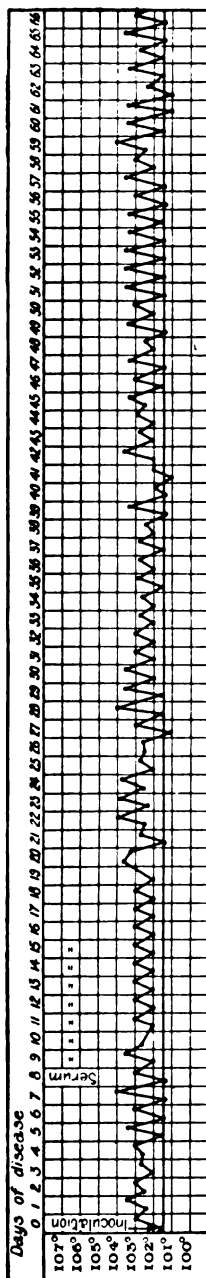
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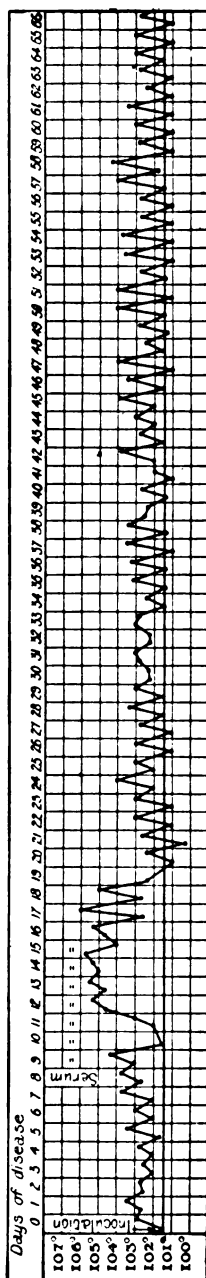


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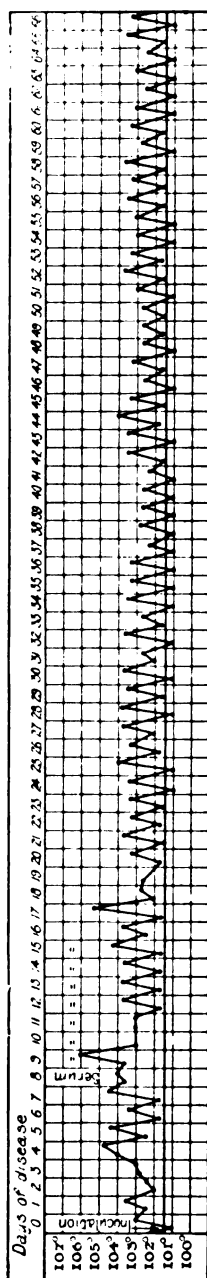


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A NOTE ON SO-CALLED "METASTATIC PULMONARY CEREBRAL ABSCESS."

By H. C. CAMERON, M.B., B.C.

WHILE it had long been known that cerebral abscess is an occasional sequel of chronic suppuration in the thoracic cavity, Sir William Gull, in the Guy's Hospital Reports for the year 1857 (S. iii., Vol. iii.), was the first to lay especial stress upon the association. He pointed out the comparative frequency of these so-called "metastatic" cerebral abscesses, and he noted how seldom is there coincident suppuration in the liver, spleen, kidney or elsewhere. The name "idiopathic" cerebral abscess he regarded as incorrect and mischievous. Every abscess in the brain, he maintained, is secondary to some focus of suppuration, near or distant, and to term any abscess idiopathic meant no more than that the search for that focus had been unsuccessful. In many cases, he pointed out, the distant focus would be found in chronic suppuration within the thorax—an old empyema, an abscess in the lung, or a bronchiectatic cavity. Since that time, classifications of cerebral abscess have been arranged with this idea in view. Thus, Dr. Newton Pitt, in his Goulstonian Lectures for 1890, divides 52 cases as follows:—

Local Lesions.—

Ear Disease	} 31
Traumatic	
Other Local Causes	

Distant Suppuration—

Pulmonary	8
Pyæmic	9
Indeterminate	...	4

The frequency of cerebral abscesses which have resulted from suppuration in the thoracic cavity is such that they are held to be a separate class, the result not of pyæmia, but of metastasis. The study of the present series of cases was undertaken to determine whether the distinction was of words only or real, and not without bearing on treatment and prognosis.

The process which results in the extension of suppuration to the brain cannot differ from that of pyæmia generally. Presumably local thrombosis of the pulmonary vessels takes place in the neighbourhood of the suppurating focus ; an infected piece of clot passes by a main pulmonary vein to the heart, and thence by the carotid artery to the brain. In one such abscess Boettcher has shown the presence of lung pigment (West : *Diseases of Organs of Respiration*. Vol. ii., p. 710). The difficulty is to find some explanation for the uniformity with which the infected clot chooses the path to the brain and avoids the route to the rest of the body. For, after careful search, I have been able to find only one example, and that a doubtful one, of generalised pyæmia secondary to suppuration in the lungs and pleura. In this connection it is interesting to note that the reverse journey seems equally easy of accomplishment, for 70 per cent. of Dr. Pitt's cases of thrombosis of the cerebral sinuses secondary to otitis media died with pulmonary infarction. Yet however this extraordinary liability of the brain to metastatic suppuration in pulmonary abscess is to be explained, it is safe to infer that the process does not differ inherently from pyæmic metastasis generally, and if the distinction is to be upheld the difference must be clinical, a difference in symptoms or in prognosis rather than in ætiology.

Pyæmic cerebral suppuration installs itself so insidiously that the condition is frequently discovered only after death. Convulsions, local or general, paralysis, optic neuritis, even headache, are all, as a rule, absent, and in the general decline of the bodily functions it is natural that the more rapid blurring of the intellect, and the slow passage of drowsiness into coma should be overlooked. It is true that there do occur cases presenting symptoms which, in the case of tumour, we should call localising

symptoms, and these at times most characteristic and insistent. Yet if the pyæmic origin of the cerebral condition is obvious, the condition is hopeless, and surgical intervention unjustifiable. For not only are pyæmic cerebral abscesses, as a rule, multiple, but they are accompanied by suppuration in other parts—in the spleen, liver, or kidney. In the following case the localisation was perfect, but operation would have been useless:—

1896. Guy's Hospital Post-mortem Reports. No. 142.

Male.—March 30th. Felt ill and sick. April 7th, 8th, 9th. Rigors. He was admitted to the South Eastern Fever Hospital as a case of typhoid fever.

April 16th. Admitted to Guy's Hospital, where a liver abscess was found, the pus from which was reported to be sterile.

April 22nd. Right leg and arm paralysed and rigid. Ptosis of the right eye, and the right pupil larger than the left.

April 23rd. Movements of the right arm and leg.

April 26th. Death.

Post-mortem.—An abscess in the left hemisphere was found, the size of a walnut, containing light green pus, situated just behind and below the upper extremity of the fissure of Rolando, and visible only on the inner surface of the brain hemisphere. Several other abscesses, varying in size from a pea to a walnut, were also found, the largest in the right hemisphere in the posterior part of the lenticular nucleus. There were also multiple abscesses in the lungs and liver, and an abscess around the cæcum. The origin of the pyæmia was found in the vermiform appendix, which was lying in a large abscess cavity passing up behind the cæcum, and through which an iron nail had ulcerated. The nail was found free in the abscess cavity.

Such is an example of a pyæmic cerebral abscess which showed, as a certain proportion of these cases do, symptoms of cortical irritation, symptoms which in the case of an abscess following otitis media, would have been called localising symptoms, and would have held out hopes of a successful evacuation of the pus. In pyæmic cerebral abscess there can be no such hope, for

the abscess in the brain is seldom single, and there is almost invariably suppuration in other parts. If "metastatic" pulmonary cerebral abscesses resemble pyæmic abscesses in these particulars, in the onset so insidious as often to defy diagnosis, and in the tendency to be multiple, the distinction can hardly be of great importance; but if a noticeable proportion have well-marked symptoms, and if a noticeable proportion are single and not multiple, then the distinction is valuable, and should be preserved. For it would then imply that, while pyæmic abscess must always prove fatal, in these metastatic abscesses an exploratory operation should be recommended and practised with the hope of a possible cure.¹

The following case was reported by Sir William Gull, in the *Guy's Hospital Reports for 1857*, S. iii., Vol. iii. :—

Male, 34. Sudden seizure with vertigo, faintness and loss of power on left side. No unconsciousness at the time. Complete recovery followed, and the patient had good health for some months afterwards. Then sudden clonic spasms of the right arm occurred, lasting a few moments and returning several times within a few hours, again with no loss of consciousness. On the following day there was some spasm of the arm, beginning as before, but the attack becoming epileptiform. On the fourth day, the epileptiform convulsions returned, followed by partial hemiplegia of the right side, gradually becoming complete. Death followed three weeks after the second seizure.

Post-mortem.—A large encysted abscess was found in the posterior lobe of the left cerebral hemisphere. The cause of this abscess was found in an old suppurating cavity in the right lung,

¹ Speaking of these abscesses, Mr. Godlee (*Diseases of the Lungs*: Fowler and Godlee; p. 617) says: "They are seldom amenable to surgical treatment. I have opened one without good result, probably because it was not single, and I have searched for one which appeared to give positive evidence of being situated in the motor area, but was really in the occipital lobe. Whilst writing this chapter, I was hesitating whether to explore a case without localising symptoms, in which, after death, no less than seven different foci of suppuration were found. Still, if distinct localising symptoms are present, the surgeon's duty is clear; he must endeavour to open the abscess, for if unrelieved the fatal result is inevitable."

which "had resulted from an attack of pneumonia three years previously."

Presuming that the pulmonary condition was not in itself incompatible with life, to empty the cerebral abscess would have been good surgery. If this case stands alone, or nearly alone, then the distinction between metastatic and pyæmic abscess is not one of first-rate importance. The name "metastatic" would then possibly be useful, because it would remind us that abscesses, dependent on pulmonary suppuration, appear most commonly in the brain, and in the brain alone, but it would not indicate a separate class of abscess different in cause, character, symptoms and prognosis. It would imply only a clinical sequence, a little less constant than the multiple hepatic abscesses in portal pyæmia, a little more constant than the suppurative pericarditis of pyæmia due to necrosis of the long bones in children.

The Guy's Hospital Post-mortem Records from the year 1876 to the year 1904 have been searched, with the following result:—Ninety-seven post-mortem examinations have been made in cases of cerebral abscess. These may be tabulated as follows, and the figures compared with Dr. Pitt's series compiled from the same source in 1889:—

Due to local causes or to causes					Dr. Pitt's series.
not determined	81	39
Pyæmic	10	8
Metastatic	6	9

Thus it will be seen that secondary suppuration appears relatively much less frequently in the present series. This is especially marked in the statistics of the last ten years, due no doubt to the increasing rarity of pyæmia and undrained empyemata. From 1876 to 1894, inclusive, there were forty-five cases of cerebral abscess, of which eight were pyæmic and four were secondary to pulmonary suppuration. In the last ten years, from 1895 to 1905, there have been fifty-two cases, of which two were pyæmic and two secondary to pulmonary suppuration.

In the ten cases of pyæmic cerebral abscess the primary focus was found in the following situations :—

1. Periostitis of tibia.
2. Periostitis of scapula.
3. Gonorrhœal stricture and peri-urethral suppuration.
4. Thrombosed prostatic veins and liver abscess.
5. Dysenteric abscess in liver.
6. Old heart disease and recent vegetations on valve.
7. Purpura hæmorrhagica.
8. Cancer of œsophagus.
9. Perforation of appendix cœci.
10. Abscess in bronchus.

The tenth case of this list is of some interest, because it is the only case with the primary focus in the thorax which gave rise to abscesses outside the brain. As the interpretation of the post-mortem findings was doubtful it may be given in full.

F. C., 23, a policeman, was admitted into Guy's Hospital, under Dr. Taylor (John ward), in 1889.

January 17th. He had diffuse general pain, and rigors, with vomiting.

January 24th. He had three fits, with rigidity and twitching.

" 30th. Rigidity of left arm.

February 2nd. Optic neuritis well marked.

" 4th. Death in coma.

Post-mortem.—Pus was found under the dura mater, due to the rupture of a cerebral abscess. There was an abscess in each frontal lobe, and an abscess in the right temporo-sphenoidal lobe which had burst into the right ventricle.

The *Liver* showed two or three well-defined patches of congestion, and on cutting across one of these pus oozed out.

The *Portal Vein* showed, in one of the secondary divisions of the right branch, a clot breaking down into pus, and from this suppuration had extended into the infected area. The remainder of the vein appeared healthy.

The *Spleen* showed a single small abscess. The internal ears, the hip and shoulder joints, the bladder, gall-bladder, urethra, and intestines were all normal.

There was a small opening into the right bronchus, near the bifurcation, which led into an abscess due to a suppurating mediastinal gland.

Note by Demonstrator.—"The cerebral abscess and the splenic abscess were regarded as pyæmic. What, then, was the cause of the general pyæmia? Was it the abscess communicating with the bronchus?"

If this question is to be answered in the affirmative, this case furnishes the only instance of general pyæmia resulting from a primary focus in the thoracic cavity.

The six cases of "metastatic" abscess, together with eleven from other sources, have been compared and examined with the following results:—

Primary Disease.—

Following on empyema	7
on gangrene of lung after pneumonia	...				4
on bronchiectasis		2
on chronic abscess of lung			4

R. Nather (*Deutsches Archiv. für klin. Med.* xxiv., p. 169) is responsible for the statement that, in diseases within the lung substance capable of causing it, cerebral abscess appears to occur in about 8 per cent.

No case followed tuberculosis of the lung, and this agrees with a statement by Sir William Gowers (*Diseases of Nervous System: Brain Abscess.* Vol. ii.).

Site.—The commonest situation was in the posterior lobe. The cerebellum was affected twice only, Case 5 and Case 14. This is in marked distinction to pyæmic abscesses which occur more frequently in the cerebellum than in any other part (Pitt. *Gulstonian Lecture*, 1890).

Sex.—There were twelve males and five females, showing a preponderance in males which has been noticed before. In Dr. Pitt's cases only one was a female.

<i>Age.</i> —In 1st decade	No cases.
2nd „	5 „
3rd „	5 „
4th „	3 „
5th „	2 „
6th „	3 „

Number of abscesses.—In six cases the abscess was single, a slightly smaller proportion than is given by Gowers, who says, “in half the cases the abscess is single” (cases 3, 8, 9, 11, 12, 16).

In cases 1 and 10, two abscesses were present, situated close together. In case 1, the report states that “it is doubtful whether a trephining over the Rolandic area would have evacuated both abscesses.” In case 10, Dr. Cayley expressly states his belief that “they might have been evacuated during life by trephining.”

Localising symptoms of one sort or another were present in thirteen cases; absent in four. Of these, only in case 13, quoted later at length, were the symptoms of a definitely misleading character, but in five others there were multiple abscesses present, which would have rendered operation useless. Of the remaining seven cases (including cases 1 and 10 mentioned above, where there were two abscesses situated in close proximity), in case 9, and in case 11, the localising symptoms only appeared a short time before death, too late to permit of the chance of a successful evacuation of the pus.

No localising symptoms, or localising symptoms too late	6
Numerous abscesses present, although localising symptoms were true	5
Numerous abscesses present, and localising symptoms misleading	1
						<hr/> 12

Thus of the seventeen cases on one or other count twelve must be dismissed as cases in which operation would have been impracticable or futile, while in five only could there have been hope of possible success.

Case 13, in which the localising symptoms were entirely misleading, is of sufficient interest to be quoted at greater length. That symptoms of cortical irritation are untrustworthy localising guides in cases of cerebral abscess has frequently been noted. Thus Huguenin, in the *Cyclopædia of the Practice of Medicine*, Vol. xii., p. 786, says, "In this respect an extraordinary want of clearness still exists, and many observations appear entirely incomprehensible. It is in the consideration of abscess in the brain, therefore, that many authors have found opportunity to shake the apparently firm physiological laws. Great collections of pus have been found in spots of which it is known that every other lesion causes a paralysis of the opposite side."

L. H., 60, admitted into Guy's Hospital March 31st, 1906, under the care of Dr. Hale White. He was operated on the same day, and a large empyema of the left side was opened and drained.

On May 9th, he left Guy's Hospital for a convalescent home.

On June 5th, he was readmitted, complaining of several transitory fits of unconsciousness at night, in which he passed urine, and of loss of power in the right arm. On examination the right arm was found to be entirely paralysed, with the exception of a little movement of the shoulder. The right leg was weak, with an increase of the knee-jerk and extensor plantar reflex; the empyema wound still discharged pus. After admission he had numerous convulsive seizures. The twitching always began in the right thumb and passed up the arm, and finally involved the leg. Consciousness was lost, but the fits never spread to the opposite side. Between the fits the paralysis was just as marked as at the time of admission. Not unnaturally it was thought that the left cerebral cortex in the Rolandic area was affected, and the question of operation was discussed. No operation was performed, and the patient died on June 21st, comatose. There had been no optic neuritis, and to the last the left side was not affected.

Post-mortem.—The brain showed multiple large abscesses in the right cerebrum, involving the Rolandic area, with secondary meningitis and pus in the ventricles. There was a single abscess in the left frontal lobe, at the extreme anterior end; although the weakness and convulsions were confined to the right side, the left Rolandic area was apparently not involved.

In such a case, a knowledge of anatomy and physiology does not greatly help. Even if we suppose that the convulsions were excited from the relatively healthy cortex by increased pressure, we have still to explain the presence of paresis on the right side and the absence of paresis on the left.

Conclusions.—A study of these cases shows that, while the prognosis of cerebral abscess secondary to suppuration in the lung or in the pleura must always be extremely bad, there still remains a percentage of cases in which operation may be undertaken with a hope of success. The name "metastatic pulmonary cerebral abscess" finds justification in the uniform absence of suppuration in other organs, in the frequency of localising signs of one sort or another, and in the number of cases in which the abscess is single. On this showing it is right to remove them from the class of pyæmic cerebral abscess where operation must invariably prove futile, and the issue must always be death.

Symptoms and History.	Localising Symptoms.	P.M. Findings.	Remarks.	Source.
<p>1.—A. E., Male, 39 years old ... 1894.—Pleurisy.</p> <p>1897.—Expectorated a cupful of foul-smelling sputum every morning. Many physical signs in chest.</p> <p>1906.—Chest explored for empyema unsuccessfully.</p> <p>Aug. 26th.—Convulsions of right arm and leg, spreading to left side. Power not lost. T. 100.4°.</p> <p>Aug. 29th.—Aphasia.</p> <p>Aug. 30th.—Twitching of left arm and face. Incontinence of urine and feces.</p> <p>Sept. 2nd.—Death, with severe bronchitis.</p>	<p>There was twitching of right arm and leg seven days before death. Five days later the left side was also affected.</p>	<p>In the left cerebral hemisphere were two abscesses—one over the leg area of the Rolandic area, one below—behind this. At the base of the left lung was a cavity, the age of which was doubtful. It was surrounded by a gangrenous pneumonic condition. Under the left scapula was a large abscess apparently external to the chest wall. There was no empyema. The right pleura was normal.</p>	<p>It was doubtful whether the superficial abscess and the cerebral abscess were truly secondary to the pulmonary condition. The abscess was not single, and it was doubtful whether a trephining over the Rolandic area on the left side would have evacuated both abscesses. <i>The attempt, however, might have been made.</i></p>	<p>Guy's Hospital Post-mortem Reports, 1894.</p>
<p>2.—Female, 17 years old, with pulmonary complaint of old standing. Eight days before death, cerebral symptoms ensued. Severe headache. Death in coma.</p>	<p>Left leg convulsed and paralysed.</p>	<p>Large cerebral abscess burst into right ventricle. Two small abscesses in posterior third of left hemisphere. Cirrhosis of lung with bronchiectatic suppurating cavities.</p>	<p>The localising symptoms were true, but the abscesses at death were multiple. <i>Operation would have been useless.</i></p>	<p>Guy's Hospital Reports, vol. iii, ser. iii. Sir William Gull.</p>

Symptoms and History.	Localising Symptoms.	P. M. Findings.	Remarks.	Source.
3.—Male, 34. Three years before death he had pneumonia, followed by symptoms of suppuration in lung. Twenty-one days before death there were cerebral symptoms.	The right side (the arm especially) convulsed and power lost.	An encysted abscess in the posterior lobe of the left cerebral hemisphere.	The localising symptoms were true and the abscess single. <i>Operation might have been successful.</i>	Guy's Hospital Reports, vol. iii., ser. iii. Museum specimen 1565 ^w .
4.—Male, 26. Pneumonia followed after some time by cerebral symptoms, coma and headache.	Right side convulsed. Left side paralysed and showing occasional tonic and fro movements.	Multiple abscesses in left cerebral hemisphere. Thrombosis of sinuses.	Symptoms indicated more than one abscess. <i>Operation contraindicated.</i> There was no abscess on the right side, though there was left-sided paralysis.	British and Foreign Medical Review, No. lxx., p. 404. Ogle.
5.—Male, 23. Signs and symptoms of abscess in lung. Cerebral symptoms thirty days before death.	Right side paralysed. No convulsions or twitchings.	Multiple. Two abscesses in right hemisphere; three or four abscesses in the left, one in cerebellum.	Localising symptoms true, but abscess multiple. <i>Operation would have been useless.</i>	Ibid.
6.—Male, 18. Empyema. Five or six weeks afterwards headache, vomiting and rise of temperature.	Left hemiplegia and strabismus.	Multiple suppurating foci in brain. Two large abscesses in right side, one of which had burst into ventricles.	The localising symptoms were true, but the abscesses were multiple. <i>Operation would have been useless.</i>	Guy's Hospital Post-mortem Reports, 1876. Path. Society Transactions, 1876-1877.

Symptoms and History.	Localising Symptoms.	P. M. Findings.	Remarks.	Source.
7.—Male, 31. Admitted under Dr. Goodhart to Guy's Hospital. April 10th.—Emphysema. June 13th.—Convulsions. June 18th.—Left side twitching. The right side was trephined, but no pus was found.	Three tracts of the needle marked by petechiae in the right cerebral cortex. One had missed pus by a bare quarter of an inch, but the pus was so thick that it would probably have refused to flow out of a cannula. Three abscesses found on the right side, two on the left, without pyogenic membrane. Old empyema on left side. Pus in bronchial tubes.	Left side twitchings.	Localising symptoms correct, but the abscesses were multiple. <i>Operation unsuccessful, and could never have been successful.</i>	Guy's Hospital Post-mortem Reports, 1888, No. 211.
8.—Female, 20. Cerebral symptoms for three weeks before death, following on symptoms of lung disease.	Single encysted abscess in cerebral cortex. Old empyema.	Convulsive movements without loss of consciousness. No loss of power.	Report incomplete, but the symptoms presumably were localising, and operation might have saved life.	St. Bart's Post-mortem Reports, 1880, vol. 5.
9.—Female, 28. A very fat woman, weighed 18 or 19 stone. Feb. 9th, 1888.—Vomiting took place on nutrient enemata. In March she had better health, but in April severe headache was complained of. April 21st.—Coma. 24th.—Convulsions of right arm just before death.	Twitching of right arm just before death.	Old abscess in left hemisphere, single. It involved the external capsule, lenticular nucleus. Old cavity at base of left lung. Pneumonic consolidation around.	The abscess was single, and localising signs were true. These occurred, however, too short a time before death, so that operation was impossible.	Guy's Hospital Post-mortem Reports, 1888, No. 130.

Symptoms and History.	Localising Symptoms.	P. M. Findings.	Remarks.	Source.
10.—H. P., Male, 19. Three years before had pleurisy. Ever since he had had occasional hemiplegia. Cerebral symptoms followed.	Left arm and leg paralysed. Clonic convulsions in left leg, spreading to arm. No loss of consciousness. At height of convulsion a little twitching on the opposite side.	Two cerebral abscesses in centrum ovale. Left lung, lower lobe showed fibrous, bronchiectatic thick-walled cavities with stagnating secretion.	"I believe," says Dr. Cayley, "if the nature of the case had been recognised during life the pus might have been evacuated by trephining, but owing to the hemiplegia and pulmonary cavitation, a diagnosis of tuberculous tumour was made."	Trans. Path. Society of London, vol. 35, 1884.
11.—S. N., Female, 19. ... Sept. 18th, 1880.—Empyema opened. The tube remained in position till Aug. 29th, when an attempt was made to remove it. Sept. 4th.—Headache, vomiting, neuro-retinitis. Drowsy.	Convulsions on left side just before death.	Left pleura half inch thick. Abscess in left posterior lobe walls one-eighth-inch thick.	The abscess was single, but the localising symptoms were delayed until just before death, too late for successful operation.	Trans. Path. Society of London, vol. 35, 1884.
12.—Female, 46. An empyema which dated from parturition four months before. Operation three days before admission. She became hemiplegic, with paralysis of the 5th and 6th nerves, on right side. She died five days afterwards.	Right hemiplegia and paralysis of right 5th and 6th nerves.	Pus in right pleura. An abscess in the left temporo-sphenoidal lobe, with pus in the left lateral ventricle and secondary suppurative meningitis.	The localising symptoms were true, and an operation undertaken immediately might have saved life.	West. Lancet, ii., 1885, p. 511.

Symptoms and History.	Localising Symptoms.	P.M. Findings.	Remarks.	Source.
13.—Male, 60. Emyema. Six weeks later fits. Paralysis and cloni: convulsions of right arm and leg. Loss of consciousness during fits.	Clonic convulsions and paralysis of right arm and leg. Left side never affected.	Pus in left pleura. Multiple abscesses in right side of brain. One abscess in left frontal lobe. Left Rolandic area not involved.	The localising symptoms were misleading, and operation would have been useless.	Dr. Hale White's Case.
14.—Male, 56. Lung symptoms for seventy days, and brain symptoms, drowsiness, coma, and vomiting ten days.	None	Multiple abscesses in cerebellum and cerebrum. Thrombosis of right femoral vein. Purulent infection of lung.	Operation impossible ...	St. Bart.'s Post-mortem Reports, 1880, vol. 3.
15.—Male, 30. Ill for two days only with cerebral symptoms. Died comatose.	None	Multiple abscesses in right cerebral hemisphere. Old cavity at apex of right lung.	Operation impossible ...	Ibid.
16.—Male, 23. Chronic disease of right pleura. Symptoms of cerebral disease for three months. Headache and drowsiness.	None	Single abscess in posterior lobe of left cerebral hemisphere.	Operation impossible ...	Guy's Hospital Reports, vol. iii. ser. iii. Sir William Gull.
17.—Male, 50. History of cough, etc. Became suddenly blind on April 25th, 1894. April 26th. Convulsions and death.	None	Old abscess in right occipital lobe with thick walls. Large superficial abscess in left frontal lobe. Old abscess cavity in left lung, with thick walls.	Operation impossible ...	Guy's Hospital Post-mortem Reports, 1894, No. 142.

(Read before the Royal Medical and Chirurgical Society.)

OBSERVATIONS ON A CASE OF CHYLURIA OCCURRING IN ENGLAND.

WITH A REPORT OF THE POST-MORTEM
EXAMINATION.

By ARTHUR F. HERTZ, M.A., M.D. OXON., M.R.C.P.

(From the Physiological Laboratory.)

CASES of chyluria are exceedingly rare in England and other temperate countries. In the last nineteen years there has only been a single case in the medical wards of Guy's Hospital, and I have been able to find in the literature only forty-six other cases which were supposed to have originated in Europe. I was therefore glad to avail myself of the permission kindly given me by Dr. Newton Pitt to investigate a case of chyluria which was in Guy's Hospital under his care in October, November, and December of 1906.

The patient was a sailor, sixty-six years old. He was thus older than any of the previously recorded cases with the exception of Byrom Bramwell's (29), who was also sixty-six, the ages of the others varying between thirteen and fifty-seven. His last voyage to the tropics was in 1886, when he spent a fortnight in India, during which he had a slight attack of "fever."

Since that time he had enjoyed good health, but for the last four years had been troubled with some dull pain in the loins. In March, 1906, he first passed milky urine. He continued to do this without intermission until his admission into Guy's Hospital in October. His appetite remained good, but it was not excessive. In June, 1906, he weighed ten stone ten pounds; in November he only weighed nine stone. In spite of this he remained fairly active and vigorous.

His symptoms were typical of those generally observed in cases of chyluria. The aching pain in the loins and loss of flesh have been noticed in most cases. In the majority there has been more marked weakness, but several patients have lived for many years without becoming completely incapacitated.

Prout (1) in 1841 noted that the disease occurs much more frequently in the tropics than in Europe. Over thirty years later the explanation of this was shown by Wucherer and Lewis to be the frequent association of chyluria with infection by *filariae*.

Among the forty-six cases described as European, which I have collected (Table I.), eight had been in some tropical country at periods varying between ten and thirty-six years before the onset of the disease. Of the remaining thirty-eight patients twenty are specifically stated to have never been abroad. These statistics suggest that a number of the cases, including the present one, which apparently originated in Europe, may have been due to infection with *filariae* during residence in some tropical country.

In ten of the cases, described since Lewis' discovery in 1872, *filariae* were looked for but not found, though one had lived in Algeria twenty-six years before the onset of the disease, and another in Mauritius thirty-six years before.

I made a very careful search for *filariae*, both in the blood and the urine of this patient, with a negative result.

I also employed the method introduced by Stäubli,¹ by means of which he succeeded in finding trichina embryos in the blood

¹ Deutsch. Arch. f. klin. Med., lxxxv, 286, 1905.

TABLE I.—Cases of non-tropical chyluria.

No.	Author.	Reference.	Sex.	Age at onset.	How long before onset was patient in the tropics, and where?	Filaria in blood or urine.	Remarks.
1	Prout*	Stomach and Renal Diseases, 3rd. edit., 1841	—	—	—	—	—
2	Golding-Bird	London Med. Gaz., xxxiii, p. 110, 1843	F	35	—	—	—
3	Bence Jones	Med.-Chir. Trans., xxxiii, 1850, and xxvi, 1853	M	32	Trinidad, 22 years	—	Slightly diminished by abdominal belt. Much improved by gallic acid 3j a day.
4	Beale	Urine and Urinary Deposits, p. 269, 1853	F	50	Never	—	—
5	Elliotson	Med. Times and Gaz., 1857, ii, p. 288	F	38	India, 10 years	—	—
6	Begbie	Edin. Med. Journ., viii, p. 132, 1862	M	21	India, 17 years	—	—
7	Ackerman	Deutsch. Klinik, 1863, p. 221	M	40	Brazil, 18 years	—	—
8	Eggel	Deutsch. Arch. f. klin. Med., vi, p. 421, 1869	F	57	Brazil, 18 years	—	—
9	Oehme	Ibid., xiv, p. 262, 1874	M	50	Never	—	Died. Carcinoma of stomach. Disappeared during pregnancy.
10	Pavy	Personal communication. (Under observation in 1876)	F	35	"	—	—
11	Glazier	Lancet, 1877, i, p. 909	M	57	"	—	Diminished by pressure over lumbo-sacral promontory; apparently also by intravesical injection of ferric chloride.
12	Dickinson and Ord	Path. Soc. Trans., xlix, pp. 391 and 402, 1878	F	20	"	None	Died. No trace of filariae and no obstruction to thoracic duct found post-mortem.
13	Osler	Personal communication.	M	—	—	—	—

* Prout records fourteen cases, eight of which were natives of hot climates, or had lived for many years in the tropics; he does not say whether any of the remaining six had been for shorter visits to tropical countries, but one of them appears to be the same case as Elliotson's (No. 5).

TABLE I.—Cases of *non-tropical chyluria*—continued.

No.	Author.	Reference.	Sex.	Age at onset.	How long before onset was patient in the tropics, and where?	Filaria in blood or urine.	Remarks.
14	Morrison	Path. Soc. Trans., xxix, p. 894, 1878	F	56	Algeria, 20 years	None	—
15	Brieger	Charité-Annalen, vii, p. 257, 1882	M	23	Never	—	—
16	Siegmund	Berl. klin. Woch., 1884, p. 150	M	45	"	—	—
17	Roberts	Urinary and Renal Diseases, p. 363, 1885	M	45	"	—	Died. Pulmonary tuberculosis, dilated lymphatics in abdominal wall.
18	Senator	Charité-Annalen, x, p. 307, 1885	F	35	Various parts of America, but probably in no filarial district, 13 years	—	—
19			M	46		None	Chylous ascites.
20	Francotti	Ann. de la Soc. Méd.-Chir. de Liège, 1886. Quoted by Saundby, <i>loc. cit. infra</i>	F	Young	Never	—	Appeared at each pregnancy, absent in intervals.
21	Huber	Virch. Arch., cvi, p. 126, 1886	M	48	—	—	—
22	Lachowicz	Rozprawz der Akad. der Wissenschaften: in Kraken. Quoted by Franz and Stejskal	F	54	Never	—	—
23	Newton Pitt	Unpublished (in Guy's Hospital, 1887)	M	51	"	None	Died. Granular kidney and tubal nephritis.
24	Goetze	Die Chylurie, Jena, 1887	F	21	"	—	Well-compensated mitral insufficiency.
25	Berri	Speriment. Firenze, viii, 114, 1890. Quoted by Franz and Stejskal	F	—	—	—	Began in 8th month of pregnancy, disappearing immediately after parturition.
26	Myers	Brit. Med. Journ., 1890, ii, p. 627	F	27	Never out of U.S.A.	None	Dilated lymphatics in skin of left thigh.

TABLE I.—Cases of non-tropical chyluria—continued.

No.	Author.	Reference.	Sex.	Age at onset.	How long before onset was patient in the tropics, and where?	Filaria in blood or urine.	Remarks.
27	Moscati	1895. Quoted by Predtetschensky, <i>loc. cit. infra</i> .	—	—	—	<i>Eustrongylus</i>	—
28	Daggett	Brit. Med. Journ., 1896, ii, p. 1706, and personal communication	M	49	Never	None	Died 1907 from an accident; chyluria gradually disappeared, and absent last few years of life.
29	Byrom Bramwell	Ibid., 1897, ii, p. 261	F	66	Mauritius, 36 years	"	—
30	Phillips	Ibid., 1898, ii, p. 1431	M	13	—	"	—
31	Vieillard	Journ. de Pharm. et de Chemie, p. 53, Paris, 1899. Quoted by Franz and Stejskal	F	40	—	—	Began after last pregnancy; lasted 20 years.
32	Predtetschensky	Zeits. f. klin. Med., xl, p. 84, 1900	F	16	Never out of Russia	Ova of <i>Taenia nana</i> in urine	—
33	Saundby	Lectures on Renal and Urinary Diseases, p. 202, 1900	F	Young	—	—	Pregnant, <i>vide</i> footnote, p. 107.
34	Waldvogel and Bickel	Deutsch. Arch. f. klin. Med., lxxiv, p. 511, 1902	F	89	Never	None	—
35	Franz and Stejskal	Zeits. f. Heilkunde, xxiii, p. 441, 1902	M	23	"	—	—
36	Gabbi	Policlinico, xi, M., p. 389, 1904	F	34	—	—	Improved by urotropine.
37	Giordano	Riforma Medica, xxi, p. 1297, 1905	M	31	Never	None	Tuberculous testis.
38	Port	Zeits. f. klin. Med., lxx, p. 455, 1906	M	63	"	"	Died. Tuberculous mediastinal glands.
39	Theilemann	Inaugural Dissertation, Halle, 1906	M	32	"	—	—
40	Hertz	Med.-Chir. Trans., 1907	M	66	India, 20 years	None	Died. Obstruction thoracic duct; purulent pericarditis.
41	Salkowski	Berl. klin. Woch., 1907, Nr. 2	M	17	—	—	—

for the first time. I drew 10 c.c. of blood from a vein by means of a syringe, and at once mixed the blood with 100 c.c. of 0.3 per cent. acetic acid, which dissolves red corpuscles, but has no injurious effects on leucocytes or parasites. On centrifugalising and preparing films from the deposit, microscopical examination showed a field filled with leucocytes only. No parasites were found either in the blood taken during the day or at 12.30 a.m.

A differential blood count showed the absence of eosinophilia—additional evidence that no living filariæ were present in the patient's body.

Physical and chemical properties of the chylous urine.—Golding-Bird (2) was the first to point out that the fat of chylous urine is not present in the form of oil globules, but as exceedingly minute "molecular" particles, resembling the "molecular basis" of chyle. A similar condition was present in this case, thus distinguishing it from the lipuria occurring in renal disease and after fractures, in which obvious fat droplets are present.

Leucocytes were invariably present, as Morrison and most later observers have also recorded. Morrison found, in addition, a few red blood-corpuscles, which were sometimes present in Gabbi's (36) case in sufficient numbers to give the urine a pink colour.³ I was never able to find any in this case. A small number of epithelial cells were generally present in the centrifugalised deposit.

A few fibrin shreds were always present, though whilst the patient was in the hospital his urine never clotted into a gelatinous mass like blanc-mange—an event which he described as having sometimes occurred before his admission. The fibrin shreds were never large enough to cause any difficulty on micturition whilst the patient was under observation, but on several occasions before he came to the hospital intravesical coagulation appears to have occurred, a considerable effort having been required to get rid of the clots present in the bladder.

³ Thus the presence of blood is not confined to tropical cases, as some writers have maintained.

No casts were found; this is in agreement with the observations of all previous writers on the subject.

On standing, no definite creamy layer formed on the surface of the chylous urine, and none separated after an hour's centrifugalisation. Golding-Bird (2) and several subsequent observers noted the formation of a creamy layer on standing, but in Brieger's (15) case, as in this one, none was present.

Warming the fluid led to the production of a film on the surface exactly similar to the "skin" of milk. This is just what would be expected from the observations made on the subject of the formation of the skin on warmed milk by Mr. R. Jamison and myself.* We showed that it was not due to a peculiar property of caseinogen, as had previously been believed, but to the universal property of proteid solutions containing fat in suspension.

The opacity of the chylous urine did not clear on shaking with ether. This, like the similar behaviour of milk, was probably due to the agglomeration of proteid molecules round the fat particles. As with milk, the opacity was completely removed by shaking with ether if the physical condition of the proteid was altered by means of an alkali. On evaporation of the ethereal extract, fat, solid at ordinary room temperature, staining with osmic acid and Sudan iii, and giving the acrolein test, was obtained.

Whenever fat was present in the urine proteid was also found; it was coagulated by heat and precipitated by nitric acid and by alcohol. The nature of the proteids was determined in the fat-free "lymphous urine" obtained by means to be subsequently described, and the results of the determination will be described in the same place.

Dextrose was never found, though repeatedly looked for, especially after meals containing excess of carbohydrate. Morrison (14) is the only observer who has found it in chylous urine.

* Journal of Physiology, xxvii, 26, 1901.

The specific gravity was, on the whole, greater the larger the quantity of fat and proteid present; it varied between 1·012 and 1·024. The urine was generally acid, occasionally neutral or alkaline, and the variations were quite independent of the quantity of fat present.

Spontaneous disappearance.—Many authors have recorded that the chyluria spontaneously disappeared for periods of various length, only to return again without any obvious cause.⁴ In the present case from October 14th to 21st there was no chyluria, although no special treatment had been adopted. Exercise and a very fatty diet had not the slightest effect during this period, the urine being perfectly normal, with no fat, albumen, sugar or formed constituents. No cause could be discovered for the return of the chylous urine on October 21st.

On December 3rd a cystoscopic examination was made, and a urinary segregator was passed with the object of determining at what point in the urinary passages the admixture with chyle occurred. The patient had a meal containing a considerable quantity of fat at mid-day. At 2 p.m. the urine was distinctly chylous; at 2.30 p.m., immediately before the examination, it was quite milky. During the examination, however, no chylous urine was passed, although observations to be presently recorded showed that the maximum excretion of fat should not have occurred before about 5 o'clock, and the last traces should not have disappeared until about 9 p.m. Consequently the desired information was not obtained.

The passage of the segregator caused some hæmorrhage, and the patient had subsequently to be catheterised for retention of urine. The hæmorrhage continued to a slight extent for two days. The bladder was washed out and helmitol administered, as signs of slight cystitis developed. These quickly disappeared, the urine becoming perfectly normal by December 6th. On December 4th, however, the patient's temperature rose and signs of bronchitis, and later of pneumonia, were found; his pulse became very rapid and feeble, and the heart sounds were faint,

⁴ In Theilemann's case (39) there was an interval of nine years between the first and second attacks.

but no pericardial rub was detected. He died on December 11th. During the eight days which elapsed between the passage of the segregator and the death of the patient he received a mixed diet containing the ordinary proportion of fat. In spite of this no trace of chyluria returned, the urine being clear and free from albumen after the hæmorrhage had ceased, and the cystitis had disappeared on December 6th.

Influence of diet.—As long ago as 1850 Bence Jones (3) observed that chyluria was more marked with animal than vegetable diet, and since then most authors have referred to the connection between the disease and the nature of the food. A diet containing much fat has been found by all except Goetze (24) to increase the amount of fat in the urine, and many have noticed that the chyluria disappeared when the diet contained as little fat as possible and during starvation. Goetze alone denied the existence of such a connection. Franz and Stejskal (35) found that the increase in the fat of the urine was always associated with an increase in the amount of proteid present.

In order to study the effect of diet on the production of chyluria I obtained a specimen of the patient's urine immediately before meals, and made him pass his urine at frequent intervals afterwards. I was thus able to trace the connection more accurately than had previously been done, as others had only compared the day and night urine, or the urine passed several hours after a meal with that passed before it.

Each specimen of urine was measured, its reaction noted, and its specific gravity ascertained. Albumen was tested for, and in a few cases was accurately estimated. Part of each specimen was put in one of a series of test-tubes of exactly the same size as each other, and the relative opacity of each pair was found by comparing the brilliancy with which an electric light could be seen through them. The more opaque specimens had to be diluted two, three, or four times with water before the comparison could be made. The specimen showing the smallest trace of opacity was numbered 1, and the others were numbered up to 15, which represented the greatest degree of opacity observed. As the opacity depends upon the amount of fat present, the

TABLE II.—*Influence of Diet on Chyluria.*

*Date.	Time.	Exercise, etc.	Food.	Reaction.	Sp. gr.	Degree of opacity (= fat).	Albumen.
Nov. 7	6 a.m.	Up all day	Full breakfast	Acid	1015	3	Very little.
	6.30 "			"	—	2	Trace.
	7 "			"	1012	5	+
	8 "			"	1016	7	+
	9 "			Neutral	1017	6	+
	10 "			"	1020	10	++
	11 "			Alkaline	1022	11	++
	12 mid- day		Full dinner	Neutral	1022	12	++
	1 p.m.			"	1018	6	+
	2 "			Acid	1020	9	+
	3 "			"	1022	13	++
	4 "		Strict tea	"	1022	14	++
	5 "			"	1021	15	++
	6 "			"	1021	13	++
	7 "		Strict supper	"	1021	8	+
	8 "			"	1020	4	Very little.
	9 "			Alkaline	1018	0	0
	10 "			"	1017	0	0
	11 "			Neutral	1018	0	0
	12 mid- night			Acid	1019	0	0
Nov. 8	6 a.m.	Up all day	Breakfast with milk in tea, but no other fat	"	1021	0	0
	7 "			"	1016	2	Trace.
	8 "			Neutral	1017	5	+
	9 "			Alkaline	1019	2	Trace.
	10 "			"	1018	0	0
	12 mid- day		Strict dinner with plenty of milk pudding	Neutral	1020	0	0
	1 p.m.			"	1020	1	+
	2 "			Acid	1021	3	+
	3 "			"	1021	4	+
	4 "		Strict tea	"	1022	7	+
	5 "			"	1024	10	++
	6 "			"	1024	6	+
	7 "		Strict supper	"	1019	4	+
	8 "			"	1019	2	Trace
	9 "			Alkaline	1017	1	"
	10 "			"	1017	0	0
	11 "			Acid	1017	0	0
	12 mid- night			"	1016	0	0

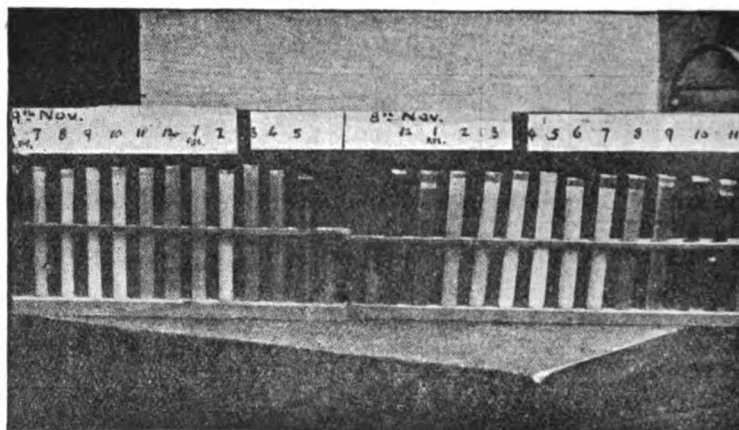
TABLE II.—*Influence of Diet on Chyluria*—continued.

Date.	Time.	Exercise, etc.	Food.	Reaction.	Sp. gr.	Degree of opacity (= fat).	Albumen.
Nov. 9	6 a.m.	Up all day	Breakfast with 20 grms. butter	Acid	1019	0	0
	6.30 "			"	1017	0	0
	7 "			"	1016	5	+
	8 "			"	1016	7	+
	9 "			Alkaline	1017	7	+
	10 "			"	1016	6	+
	11 "			—	—	3	Very little.
	12 mid-day		Almost strict dinner	—	—	1	Trace.
	1 p.m.			—	—	2	Trace.
	2 "			—	—	4	+
	3 "			—	—	2	Trace.
	4 "			—	—	1	"
	5 "			—	—	0	0
	6 "			—	—	0	0
	12 mid-night			—	—	0	0
Nov. 10	6 a.m.	In bed	Full breakfast	—	—	0	0
	6.30 "			—	—	0	0
	6.45 "			—	—	0	0
	6.55 "			—	—	0	0
	7.5 "			—	—	0	0
	7.15 "			—	—	0	0
	7.20 "			—	—	0	0
	7.25 "			—	—	Faintest trace	Faintest trace.
Nov. 12	7.30 "	In bed	Strict dinner	—	—	1	Trace.
	12 mid-day			—	—	0	0
	4 p.m.		Strict tea	—	—	0	0
	6 "		Strict supper	—	—	0	0
	12 mid-night			—	—	0	0

numbers indicate which of any two specimens contains the most fat, though, of course, not the actual amount present. Evidence of the accuracy of this supposition is given by the actual analyses made; in three specimens which had opacities represented by the numbers 6, 11, and 14 the percentage of fat present was 0.284, 0.664, and 2.170 respectively.

Table II. shows the results obtained, and Fig. 1 is a reproduction of a photograph taken of two series of test-tubes containing

FIG. 1.



Photograph of test-tubes containing hourly specimens of urine to show the relation of the chyluria to the fat in the food. On Nov. 9th breakfast with 20 grms. of butter was given at 6 a.m., and a dinner containing very little fat at 12 o'clock. On Nov. 8th a dinner with plenty of milk pudding was given at 12 o'clock, after which no more fatty food was eaten.

hourly specimens of the urine. If as little fat as possible was taken after dinner at mid-day, and the urine passed at midnight, the night's urine contained no fat and no albumen. The observations made on November 10th showed that when the patient was in bed, one hour and twenty-five minutes elapsed before the first trace of chyle appeared in the urine. A later observation, when the patient was up, showed that chyle appeared in the urine already thirty-three minutes after eating 25 grms. of butter with bread and biscuits, the patient having walked up and down immediately after the meal. Further experiments on the variation produced by exercise will be described later.

The amount of fat present in the urine increased steadily every hour up to the fifth after the ordinary breakfast, and the ordinary dinner on November 7th, and the only slightly restricted

dinner of the 9th⁶; when the meal contained only a limited quantity of fat, as with the breakfast on November 8th, and the dinner on November 9th, the maximum occurred already two hours after the meal. No more fat was given on November 7th or 8th after dinner; the disappearance of chyle from the urine occurred eight hours after the meal on both occasions. After the breakfast on the 8th and the dinner on the 9th, in both of which the fat was restricted, the chyluria disappeared after three and four hours respectively. Numerous other observations confirmed these time relations. After meals containing as little fat as possible (as on November 12th), no chyluria occurred unless much exercise was taken, in which case traces of fat appeared in the urine, as it was found impossible to devise a diet absolutely free from fat. The following diet, however, contained so little that if the patient rested an hour or two after dinner no trace of fat appeared in the urine all day: Certain fish (haddock, cod, whiting, turbot, or brill), jelly, potatoes, green vegetables and fruit, bread with jam, honey, or treacle; no milk, butter, cheese, or eggs. A single egg for breakfast was sufficient to produce well-marked chyluria, but lean beef had no effect if care was taken to avoid all the obvious fat. It is thus possible for a patient with chylous urine, who is troubled with difficulty in micturition due to intravesical clotting, to control the chyluria completely by resting after meals which are composed in the way described.

The next question to decide was whether the fat in chylous urine was the same as that taken in the food or was derived from the body stores of fat. The speed with which the appearance of the fat in the urine followed the taking of fat in the food suggested that the former was the case. This is confirmed by Huber (21) and Salkowski (41) who detected cod-liver oil in the urine after giving it to their patients, and by Franz and Stejskal

⁶ This corresponds well with Hamill's observations on a patient with a lymphatic fistula in the groin. The maximum amount of fat was found to be present six hours after the principal meal. *Journ. of Physiology*, xxxv, 151, 1906.

(35), who found that the fat in the urine had the same melting-point as the unusual fat (erucic acid) which their patient ate. They also found that the urine was coloured red after the patient had taken some olive oil stained with Sudan iii. The present patient took some butter stained deeply with Sudan iii, which did not affect its taste in the slightest degree, with his bread on two occasions; the urine passed after the meal was chylous and tinged faintly red. But as the only fat taken in the meal was deep red, and the urine was white with only a slight pink tinge, it seems probable that the compound of the fat with the stain was dissociated in the intestines. This seems to be confirmed by the fact that none of the fat particles in the urine appeared to be stained when examined under the microscope.

Diets containing excessive amounts of carbohydrates and of proteid had, in no case, the slightest effect on the urine. The former, given as bread, never produced a trace of chyluria or lymphuria, confirming the generally accepted view that carbohydrates are absorbed by the capillaries and not by the lymphatics; moreover, the conversion of carbohydrate into fat in the intestinal epithelium, which Pavy believes to occur in rabbits, does not appear to occur in man. Proteid food also never produced albuminuria, showing that proteids are probably absorbed by capillaries and not by lymphatics.

Thus, as far as food is concerned, albuminuria never occurred independently of chyluria, the variations in the amount of albumen in the urine being approximately parallel with that of the amount of fat. The ratio of the amount of fat to that of proteid present on the two occasions when both were accurately determined on November 7th gave results which fit in well with the assumption that it is actually chyle which is present in the urine. The amount of proteid in chyle is about 2 per cent.; hence when 0.885 per cent. proteid was present in the urine, 44 per cent. of the specimen was chyle and 56 per cent. urine, and when 1.885 per cent. proteid was present, 94 per cent. was chyle and only 6 per cent. urine. As the percentage of fat in the two specimens was 0.664 and 2.170 respectively, the percentage

of fat in the original chyle must have been $(0.664 \times \frac{100}{44} =) 1.5$ and $(2.17 \times \frac{100}{94} =) 2.3$ respectively. The former gives the maximum percentage of fat in the chyle after the breakfast, the latter after the dinner; as the dinner contained considerably more fat than the breakfast, the larger percentage in the chyle is explained.

Two tablespoonsful of oleic acid were given on two occasions, once alone and once with a teaspoonful of glycerine. On neither occasion did any chyluria occur; this is probably due to the fact that slight diarrhoea was produced, so that the fatty acid passed too rapidly out of the body for absorption to occur.

Influence of exercise.—A number of authors have observed that exercise increases chyluria, though generally no exact data have been given. Golding-Bird (2) stated that albuminuria was occasionally present during the fat-free periods, but was unable to give any explanation of this. The few subsequent investigators who have confirmed his observation made no statement as to the nature of the albumen, and seem generally to have regarded its presence as a sign that the kidneys were slightly diseased. I have been able to demonstrate very clearly the effect of exercise on chyluria, and to show that the albuminuria without fat is really lymphuria and due to exercise. (Table III.)

Experiments 1 and 2 show that albuminuria is produced within an hour by exercise, and that if no fat has been eaten for many hours no fat appears with the albumen in the urine. Numerous controls showed that in the absence of exercise, if no fatty food had been taken, no albuminuria was present.

Microscopical examination of the urine showed that leucocytes were present in large numbers, varying with the amount of albumen, although none could be found in the albumen-free urine passed during rest with a fat-free diet. Chemical examination showed that an albumen which began to coagulate at 69° was present; this was probably serum-albumen, the coagulation-temperature of which is from 70° to 85° . In addition a small quantity of a globulin coagulating at 56° , and rather more of

another coagulating at 75°, were present; the latter was, no doubt, serum-globulin, and the former fibrinogen, as this coagulates mainly at 56°, and a number of minute fibrin flocculi were found floating in the urine. The presence of the three proteids of lymph and of leucocytes affords very strong evidence that the urine was mixed with lymph. No ordinary cases of albuminuria are associated with fibrinuria or with such a large admixture of leucocytes.

TABLE III.—*Influence of Exercise on Chyluria.*

No.	Date.	Time.	Food.	Exercise.	Fat in urine.	Proteid in urine.
1	—	6 a.m. 6-7 "	Fasting "	— Walking	None "	None Much
2	—	10 " 11 " 12 midday	Fat-free breakfast at 6 a.m.	In bed until 10 a.m. Walk from 10 to 12	" " "	None Trace Much
3	—	8.30 a.m. 9 "	Full breakfast	Rest since 7 Walk immediately after breakfast	" "	None A little
		9.15 " 9.30 "		Continue walk " "	1 4	Much "
4	—	4 p.m. 5 " 6 "	Dinner with milk pudding but no other fat at 12, nothing since	Rest since 12 Walk from 5 to 6	5 3 6	" Less Much
5	Nov. 15	11 a.m. 11.45 "	Fat-free breakfast at 6 a.m.	In bed all the morning Right arm 3 lb. dumb-bell for ½-hour in bed	None "	None "
6	—	4 p.m. 4.45 "	Fat-free dinner at 12	In bed all day Left arm 3 lb. dumb-bell for ½-hour in bed	" "	" "

Experiment 3 shows that walking after a meal containing fat gives rise to albuminuria in half an hour, which is greatly increased in three-quarters of an hour, when chyle also begins to be present; in an hour chyluria is well marked. On another

occasion chyluria was observed as early as thirty-three minutes after the meal. With a precisely similar breakfast taken in bed and not followed by exercise, chylous urine was not passed until the lapse of one hour and twenty-five minutes.

Experiment 4 shows that exercise taken during the decline in the chyluria produced by a meal causes a secondary increase in the chyluria.

These observations can only be explained by supposing that there is an escape of lymph into the urine when the flow from the legs is increased by exercise. After a meal containing fat, chyle does not escape into the urine until a certain degree of distension of the lacteals is produced, so that if the patient remains at rest the onset of chyluria will be appreciably later than the beginning of fat absorption. But the necessary distension is already present when the absorption begins if exercise is being taken, so that the first appearance of fat in the urine—in experiment 3 three-quarters of an hour after food—indicates the moment in which fat absorption begins.

An hour's exercise with a three-pound dumb-bell, first with the right arm and then with the left, had no effect on the urine whether the patient was lying down (experiments 5 and 6) or sitting up; this suggested that the obstruction to the lymphatic system was below the point at which the lymphatics of the left arm unite with the thoracic duct, and did not affect the right lymphatic duct. As will be seen later, the autopsy confirmed this supposition.

Influence of posture.—Several authors have stated that the erect position tends to produce more chyluria than the horizontal position, but they did not realise the important part played by exercise in its production, so that their results might have been due to exercise rather than posture.

Ackerman (7), however, clearly demonstrated that his patient could entirely prevent the appearance of chyle in the urine by lying on the right side.

My own observations showed that merely sitting or standing produced neither chyluria nor lymphuria if the patient had eaten no fat food for several hours previously. After a meal

containing fat, chyle seemed to appear in the urine rather sooner if the patient was up, though not taking any exercise, than if he was in bed. The difference, however, was slight, and would alone be insufficient to prove definitely that a vertical position increased the tendency of the chyle to escape. Conclusive evidence of the importance of posture was obtained, however, when exercise was taken. When the patient, lying in bed, alternately flexed and extended the right leg on to the thigh continuously for an hour, and then performed the same movements for an hour with his left leg, no lymphuria was produced. The same movement of either leg at the same rate for only three-quarters of an hour, when the patient was sitting, produced well-marked lymphuria.

The effect of posture depends probably upon gravity, which would aid the back-flow of lymph, caused by obstruction in the thorax, when the patient is standing or sitting.

Autopsy.—I have been able to find only three published descriptions of *post-mortem* examinations of patients who had suffered from non-tropical chyluria. In Oehme's case the patient died a few days over a year after the onset of chyluria; he was a man of fifty, and had been troubled during the whole of the time with gastric disturbances. At the autopsy a carcinoma of the posterior wall of the pyloric end of the stomach was found. Nothing else abnormal was present. Though Oehme (9) does not himself suggest that the growth had any connection with the chyluria, it does not seem improbable that it pressed upon the larger lymphatics just below the receptaculum chyli, and that an obstruction to the flow of lymph out of the abdomen was produced in this way. In support of this view is the fact that the duration of the chyluria corresponded with the duration of the gastric symptoms, which were presumably the direct result of the growth.

Sir Wm. Roberts' (17) patient died of pulmonary tuberculosis. In the skin and subcutaneous tissue of the abdominal wall were some enormously dilated lymphatics from which lymph and chyle had escaped during life. No cause was found either for these dilated lymphatics or for the chyluria. But chylous urine

had only been passed on two occasions—once six and once five months before death, and the lymphatics of the abdominal walls had become less distended as the phthisis advanced, and had ceased to discharge five days before death. It was therefore hardly surprising that the cause remained undiscovered, as the obstruction to the lymphatics appears to have almost disappeared by the time the patient died.

In the case reported by Port (38) the thoracic duct was obstructed by the pressure of tuberculous glands; occasional spontaneous disappearance of the chyluria was apparently due to relief of pressure brought about by the bursting of caseous glands into the œsophagus or left bronchus. Perhaps in Roberts' case the obstruction and the final relief may have been due to the same causes.

Prof. Osler tells me that he performed an autopsy in Montreal on a patient who had suffered from chyluria; but he was unable to find any obstruction to the thoracic duct or any obvious dilatation of the abdominal lymphatics.

In addition to these four cases a post-mortem examination was made on a patient who was under Dr. Newton Pitt in Guy's Hospital in 1887. Granular kidney and tubal nephritis were found. The cause of the chyluria was not discovered, but seeing that the patient had passed no chylous urine since the symptoms of nephritis began to develop eight months before death, this is not surprising.

Dr. Fawcett kindly allowed me to investigate the condition of the lymphatics in the present case. I injected mercury at a pressure of about 25 mm. into the lymphatic system at various points. I first introduced the cannula into the thoracic duct, just below the point where it joined the angle between the jugular and subclavian veins. After the mercury had run in, the duct could be traced to the posterior thoracic wall. As the vessel ruptured at this point, it was necessary to introduce the cannula at another point just below. The mercury passed down the next part of the duct with difficulty, and even under a higher pressure it could not be forced further than a point 7 cm. above the diaphragm. On injecting upwards from the receptaculum

chyli the mercury did not pass higher than this same point. On subsequently removing the whole of the thoracic duct it was found that a fine probe, passed either from above or below, met with obstruction at the same point—7 cm. above the receptaculum chyli. By using somewhat greater force the probe was pushed through the obstruction from below, but even after this the resistance could still be felt when it was passed in either direction.

On injecting downwards from the receptaculum chyli the lymphatics behind the peritoneum were readily filled, although the injection was in the opposite direction to that of the normal lymph flow. These lymphatics appeared to be abnormally large. By injecting at two other points lower down in the abdomen the connection between the lacteals and the large lymphatics round the aorta could be traced, and two large vessels were seen passing from the lymphatics internal to the external iliac artery over the lateral pelvic wall on to the side of the bladder, where they divided into numerous branches. The lymphatics on the left side of the bladder could not be injected. There was thus a very free anastomosis between the lymphatics of the right side of the bladder and those of the intestines, which was sufficient to allow mercury to pass in the wrong direction from the receptaculum chyli to the bladder. As much of the lymph from the leg ascends in lymphatics which run with the external iliac artery, the lymph from the right leg would have had easy access to the lymphatics of the bladder, and that from the left leg had presumably to ascend to the vessels round the abdominal aorta and then descend again to the right side of the bladder.

The lymphatics to the kidneys do not appear to have been abnormally large, and the valves were still competent, as I was unable to inject them with mercury from the plexus round the aorta.

These observations strongly suggest that the obstruction in the thoracic duct had led to dilatation of the abdominal lymphatics, and that a reflux of chyle from the intestines to the right side of the bladder, but not to the kidneys or ureters, had become possible. I was unable to inject any mercury from the bladder

lymphatics into the bladder lumen; but for nine days before death no chyluria had been present, so that it may be supposed that in some way the fistulous opening had become closed, as had also occurred between the 14th and 21st of October. The interior of the bladder showed no trace of cystitis; a minute bluish papilliform projection about 2 mm. long, $1\frac{1}{2}$ mm. broad, and 1 mm. high was found on the mucous membrane at a point on the inside of the bladder corresponding to the position of the dilated lymphatics on the outside. On microscopical examination this papilliform projection was found to consist of unorganised fibrin. From the position of this peculiar papilliform mass of fibrin, which was closely adherent to the bladder surface, Mr. Targett, who kindly examined the section for me, thought that it was very probably produced by coagulation of chyle at the point where the escape into the bladder occurred.

The prostate was normal, and the urethra showed no signs of inflammation, but there was a little submucous bruising in the membranous urethra.

The kidneys were quite normal.

About two ounces of pus were found in the pericardium, and recent lymph was present on the surface of the heart. The coronary arteries were very calcareous, and well-marked atheroma was present in the thoracic and abdominal aorta.

Acute bronchitis and hypostatic pneumonia were present in both lungs.

Pathogenesis.—Two theories have been advanced to explain the origin of the European cases of chyluria. According to the older one, first propounded by Prout (1) in 1841, later supported by Eggel (8) and Brieger (15), and recently revived by Waldvogel and Bickel, the escape of fat and proteid into the urine occurs from the blood, so that "chyluria" is a misnomer. Waldvogel and Bickel (34) believe that the blood loses its power of converting the fat of chyle into soluble substances; consequently the fat accumulates in the blood and is excreted by the kidneys. But excess of fat in the blood has been found neither by me nor by any previous observer, although several, the first of whom was Bence Jones, have examined the condition of the blood. More-

over, it is impossible to explain by this theory why proteid and leucocytes should always accompany the fat in the urine. Conclusive evidence against it is given by my observations on the lymphuria produced by exercise, where there is no question of passage of fat into the urine at all. Moreover, the "molecular" condition of the fat is strong evidence that the urine is actually mixed with chyle, as a similar molecular condition occurs also in chyle, but nowhere else.

The second theory, which appears to have owed its origin to Ackerman (7) in 1868, has been further developed in connection with tropical chyluria by Manson. It has received the support of all recent writers on the subject, except those mentioned above. An obstruction to the lymphatics, somewhere between those of the small intestines and the end of the thoracic duct, is supposed to exist. As a consequence there is stasis and a rise of pressure everywhere below the point of obstruction. Owing to the dilatation of the vessels the valves become incompetent, and a rise of pressure drives the chyle from the intestinal lacteals in a retrograde direction to the pelvis, whence it passes by the lymphatics of the abdominal wall to their anastomosis with those of the upper part of the body, which join the right lymphatic duct or the thoracic duct above the obstruction. Where the dilated lymphatics are feebly supported one may rupture. If this occurs into the abdominal cavity chylous ascites results; if a distended lymphatic in the submucous tissue of the bladder bursts, lymph and chyle will escape and chyluria result. Finally, the subcutaneous lymphatics may give way, and a lymphous and chylous discharge from the skin is the result. More than one of these events may occur in the same patient, as in Senator's, who had chylous ascites as well as chyluria, in Sir William Roberts' patient, who had leakage from dilated lymphatics under the skin of the abdomen, and in Myers' patient, who had had a similar condition in the upper part of her thigh for eleven years before the onset of chyluria.

In the present case and in Port's the obstruction was actually found.⁶ In two other cases in which a post-mortem examination

⁶ An obstruction of the thoracic duct has also been found in a number of cases of chylous effusions into the pleural or peritoneal cavity.

was made none was observed, but no special means appear to have been taken to investigate the condition of the thoracic duct. In Osler's case, in spite of a careful search, no obstruction could be found.

Chyluria occurring in the tropics is always associated with infection with filariæ. According to Manson⁷ the thoracic duct becomes occluded "in some way as yet unexplained, either by mechanical plugging by a bunch of intertwined parent filariæ, or in consequence of inflammatory conditions leading to stenosis brought about by the presence of such filariæ in the vessel." The parasites have never been found in the thoracic duct, but stenosis, apparently identical in character with that of the present case, was found to be present by Stephen Mackenzie⁸ and various other authors, who found, moreover, considerable dilatation of the abdominal and pelvic lymphatics. When stenosis is once produced the obstruction will remain whether the filariæ live or not; hence the absence of the parasite from the blood and urine in the present case and in the others in which the patients had been in the tropics many years before the onset of the chyluria is no evidence that filariæ were not the original cause of the obstruction. The long period which elapsed between the supposed original infection and the onset of chyluria is only analogous to the many years which may elapse before dilated hæmorrhoidal veins rupture.

In those patients who have never been abroad obstruction must be due to some other cause, such as pressure exerted from outside by caseous glands, as in Port's case, by the pregnant uterus, as in the cases recorded by Francotti (20), Berri (25), and Vieillard (31), or by artificial means, as in Saundby's case.⁹ Possibly in some European cases parasites other than filariæ may cause the obstruction. Thus Predtetschensky (32) found on

⁷ Allbutt's System of Medicine, 2nd edition, vol. ii., part ii., p. 944, 1907.

⁸ Trans. Path. Soc., xxxiii, 394, 1882.

⁹ A young unmarried woman, who bandaged her abdomen so tightly, in order to conceal her pregnancy, that severe œdema of the legs, vulva, and lower part of the abdomen resulted, passed chylous urine for some days after labour. Probably the pressure exerted by the abdominal bandage produced temporary obstruction to the lymphatics (Ref. 32).

one occasion ova similar to those of *Tenia nana*, a minute tapeworm almost unknown in England, in the chylous urine of his patient. Though no other evidence of infection with the parasite was forthcoming, Predtetschensky suggested that it might have been the cause of the lymphatic obstruction. He states, moreover, that Moscato (27) found *Eustrongylus gigas*, a worm 9 cm. long, on two occasions in the urine of a patient who was passing chylous urine, the chyluria on both occasions ceasing temporarily after the passage of the parasite.¹⁰

The chief argument against this theory is the almost constant absence of sugar from chylous urine. But Munk and Rosenstein found that human lymph obtained from a lymphatic fistula contained only 0.1 per cent. dextrose. Chylous urine must always contain less than this—and generally considerably less—owing to the admixture of the chyle with the urine. As the ordinary methods are only sufficiently delicate to recognise about 0.1 per cent. of sugar in the urine, the slight excess present in chyluria readily escapes recognition.

At the discussion in Berlin on the case reported by Siegmund (16), who believed that the chyle escaped through a fistulous opening in the bladder, Virchow argued against this explanation on the ground that no connection existed between the lymphatics of the intestines and those of the bladder. The ease with which in this case I was able to inject the lymphatics of the bladder from the upper part of the abdomen proves the error of Virchow's statement, and demonstrates that a reflux of chyle from the intestines to the bladder could have occurred.

In the present instance the fistulous connection between the lymphatic and urinary tracts appears from the post-mortem examination to have been in the bladder. Dr. Pavy, whilst the patient was still alive, pointed out to me that this was probably the case, as even when the patient was passing clots *per urethram* there had been no renal colic, though its occurrence might have

¹⁰ Stuertz found eight ova of this parasite in different specimens of chylous urine of a man, whose illness began at the age of 20, when he was living in Brisbane (Deutsch. Arch. f. klin. Med., lxxvii., p. 557, 1903).

been expected if the escape took place in the kidneys or their pelves. That the leakage rarely if ever occurs in the kidneys is rendered likely by the invariable absence of renal casts from chylous urine. Moreover, in this case, as in three of the four others in which an autopsy was made, the kidneys were perfectly healthy.

Franz and Stejskal (35), however, state that they could observe during a cystoscopic examination chylous urine escaping from both ureters; they conclude that there was leakage into the pelves of both kidneys. Salkowski (41), also states that in his case milky fluid could be seen by the cystoscope issuing from the right ureter. Moreover, the post-mortem examination in Mackenzie's case of tropical chyluria suggested, but did not definitely prove, that the leakage was into the left kidney, and Port (38), finding that the pelves of both kidneys contained chylous fluid, though the kidney tubules, which were perfectly normal, did not, believed that escape occurred in his case into the renal pelves.

CONCLUSIONS.

1. Chyluria, whether associated with filariasis or not, is always due to the same anatomical lesion—an obstruction to the thoracic duct or some of its largest tributaries.

2. The obstruction may remain for many years before rupture of a dilated lymphatic into the urinary tract occurs and chyluria results, so that all traces of an original filarial infection may have disappeared before the onset of the chyluria.

3. Chyluria depends upon the distension of the abdominal lymphatics with the chyle produced during absorption of fat from the intestines. After an ordinary meal fat appears in the urine in half an hour if exercise is taken, but in about an hour and a half if no exercise is taken. The maximum amount is present five hours after food, and the last traces disappear in eight hours. These observations suggest that fat digestion and absorption

occur more rapidly, and that the commencement of absorption is earlier than has generally been believed.

4. The increased flow of lymph from the legs produced by exercise gives rise to distension of the lymphatics, so that escape of lymph into the urine with the production of lymphuria may occur. It appears probable that such a lymphuria, though observed for the first time in the present case, will always be found to accompany chyluria.

DIPHThEROID ORGANISMS IN THE ThROATS OF THE INSANE.

(Reprinted from the Archives of Neurology, vol. iii., 1907.)

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THE pathological investigation of insanity in the past has chiefly had for its aim the determination of the histological changes caused by attacks of mental disorder. The results of such investigations have been many and important, but it cannot, we think, be claimed that these results have placed the clinician of to-day in a very much more favourable position than his *confrère* of twenty years ago.

Had the workers in the domain of general pathology been content to rest satisfied with the results obtained by histological

methods alone, it is plain that most of the modern methods at the disposal of the progressive physician would have remained undiscovered. It is, therefore, not only reasonable, but absolutely imperative, that every new means for pathological research should be adopted by those whose particular work it is to investigate the etiology of mental diseases.

In the past we have been accustomed to think of insanity as a spontaneous breakdown of the nervous system, due, for the most part, to a bad nervous heredity; and so it may be, but until we can assert without fear of contradiction that all the causes of the great bulk of insanity have been sought out and classed as unavoidable, it is the bounden duty of investigators to seek in every reasonable direction for causes which may be avoidable or removable.

Those, therefore, who are seeking by bacteriological or chemico-pathological means to discover a bacterial or toxic exciting cause for these diseases, occupy an unassailable position, and the work of Dr. Ford Robertson with which we are at the moment concerned entitles him to a place amongst the foremost of investigators pursuing this line of research. Dr. Robertson's many recent papers have pointed to the idea that a member of the diphtheria group of organisms—possibly* the Klebs-Löffler bacillus itself—may play an important part in the production of a great class of insanity—namely, general paralysis of the insane. His hypothesis is, we gather, that by syphilis, and perhaps other diseases associated with alcoholic excess and meat diet, the defensive powers of the organism are so reduced in certain directions that the individual falls a prey to the destructive action of the diphtheroid organism, which, he contends, is almost constantly associated with this class of insanity; and, further, that it is this organism or its toxin which gives the paralytic aspect to the disease.

On the other hand, he recognises that this bacillus is also present in the throats and other tissues of cases of insanity not

* In the Morrison Lectures Dr. Ford Robertson claims to have isolated a specific diphtheroid organism which he terms "*Bacillus paralyticans*." Review of Neurology and Psychiatry, 1906, vol. iv., February, March, April (Editor's Note).

having a paralytic character. That these cases do not show paralytic symptoms is probably due, he explains, to the fact that the defensive powers have not been reduced by preceding attacks of syphilis, &c. This, we believe, fairly states Dr. Ford Robertson's position.

OBJECT OF THE PRESENT INVESTIGATION.

This hypothesis by its novelty, combined with the weight of the carefully thought out arguments Dr. Robertson brings to bear upon it, is an extremely attractive one, and the issues involved are far-reaching and important. We therefore determined to investigate the conditions that obtain in some of the large asylums south of the Tweed, with special reference to the relative frequency of the presence of a diphtheroid organism in the throats of the insane, and particularly of general paralytics; and, further, to examine such fluids and tissues as were easily obtained from the cadaver of the general paralytic at the *post-mortem* inspection, with a view to the detection of diphtheroid organisms.

The investigation appeared to us to be eminently desirable in view of the possibility that the facts hitherto observed might not warrant the inferences drawn from them. We hoped that our inquiry might throw some light on the question of whether Dr. Ford Robertson had to do with a "local infection" in the asylum from which he drew his material, or whether his results in this particular held good in the case of other asylums.

In the course of our investigations we have examined 138 living cases and material from 33 *post-mortem* inspections, with a great amount of care, and have subjected those organisms which we were able to isolate to fairly critical tests. Our material has been drawn from two asylums—the one, the London County Asylum at Colney Hatch, an old-established institution; the other, the London County Asylum at Claybury, a comparatively new one. The *post-mortem* material was obtained exclusively from Colney Hatch Asylum during a period of three months ending December 31st, 1903. In this connection

we wish to express our thanks to Dr. Mott, F.R.S., at whose instigation the investigation was undertaken, and to whom the writers are indebted for much valuable advice and criticism. Also to Drs. Seward and Jones, the medical superintendents of the Colney Hatch and Claybury Asylums respectively, as well as to the medical staffs of those institutions, for so freely placing clinical material at our disposal.

As a preliminary, we deemed it advisable to ascertain the opinion of others as to the degree of frequency with which "diphtheroid" organisms could be detected in the throats of normal individuals under varying conditions. With this aim in view we have referred to a number of papers by different workers which appear to bear upon the question, and which have been published during the last decade—for we considered that by restricting ourselves to comparatively recent literature we should be able to include results in which attempts had been made to differentiate between the *B. diphtheria* of Klebs and Löffler on the one hand, and other members of that large class of organisms, including the bacillus of Hoffmann, loosely grouped under the term "pseudo-diphtheria bacillus," on the other.

TABLE I.

THE INCIDENCE OF *B. Diphtheria* IN THE NORMAL THROAT.

Name.	Total number investigated.	Number of contacts.	Percentage K.-L. B. in contacts.	Percentage Hoffmann's in contacts.	Number of non-contacts.	Percentage K.-L. B. in non-contacts.	Percentage Hoffmann's in non-contacts.
(1) Cobbett, Louis ⁴ ...	650	650	19.0	23.0	—	—	—
(2) Berry and Washbourn ⁸ ...	118	118	14.4	19.4	—	—	—
(3) Goadby ⁸ ...	686	586	32.4	16.0	100	18.00	16.0
(4) Gorham ¹⁰ ...	2,375	1,406	11.9	—	969	3.00	—
(5) Kober ¹¹ ...	723	133	84.0	—	590	15.00	—
(6) Massac. Board of Health ¹²	4,250	—	—	—	—	3.00	—
(7) Meade, Bolton ¹³ ...	214	214	45.0	—	—	—	—
(8) Müller ¹⁴ ...	100	—	—	—	100	6.00	—
(9) Parke and Bebe ¹⁵ ...	378	48	50.0	—	330	9.77	7.2

The results of our search, when averaged, showed that the true diphtheria bacillus may be isolated, by suitable means,

from the throats of nearly 7 per cent. of the presumably healthy population. On the other hand, it is found, when examining the throats of "contacts" (that is, of individuals in more or less close contact with actual cases of diphtheria) that this percentage rises to 33 or more. The authors consulted and the various figures obtained in this connection deal with observations upon nearly 10,000 individuals; and may be conveniently presented in the accompanying tabular synopsis (Table I.).

In striking contrast to the results obtained by the above observers, we find, on analysing Dr. Ford Robertson's papers, that diphtheroid organisms were obtained *post-mortem* from one or more situations in 85 per cent. of a total of twenty general paralytics he examined. Of these diphtheroid organisms we gather that he considered all were true diphtheria bacilli. A percentage incidence such as this, if it can be shown to hold good generally, certainly affords grounds for the assumption that the association of general paralysis and the Klebs-Löffler bacillus is not a mere coincidence.

TECHNIQUE ADOPTED.

(a) *Material obtained during life.*—The methods we employed for obtaining and examining our specimens may be referred to in some detail, for so much of the value of observations of this character depends upon matters of technique.

The apparatus employed for the collection of material from the throat consisted of a simple "swab" similar to that used by one of the writers for cases of suspected diphtheria for many years past. This is prepared by twisting a small piece of cotton-wool around one end of a short metal rod and placing this, wool downwards, in a clean test tube. The tube is plugged with cotton-wool, and the whole placed in a hot-air steriliser at 150° C. for an hour to ensure complete sterilisation.

In collecting the material a swab was removed from its tube and the cotton-wool-covered end pressed firmly against several different points of the fauces (special attention being directed to the surface of the tonsils, and particularly to any purulent collections in tonsillar crypts) and of the back of the pharynx,

rotating the metal rod at the same time between the thumb and forefinger. The swab was then replaced in the tube and the latter re-plugged and labelled.

Attention was also directed to carious teeth and swabbings made therefrom, but care was taken to prevent contact between the swab and either the tongue, palate, or the inner side of the cheeks.

The next step was to inoculate culture tubes, containing blood serum inspissated in the slanting position, "in series," by rubbing the swab firmly all over the sloped surface of the medium in a first tube; passing a sterile platinum loop over the inseminated surface of the serum in this tube, and with the material collected in the loop inoculating the surface of the medium in a second, and, finally, a third tube. By following this procedure, a large number of the organisms in the throat are rubbed on to the surface of the serum in the first tube; by means of the loop a few of all these organisms are conveyed to the second tube, and still fewer to the third tube. The tubes were then incubated at a temperature of 37° C. overnight, and examined early next morning—a period of about twelve to sixteen hours, never more than eighteen hours.

After incubation, the resulting growth on the first tube was usually a fairly even, moist layer over the surface of the medium, in which no discrete colonies could be distinguished. In the second tube the growth was decidedly less luxuriant, and some separate colonies were frequently apparent. In the third tube, however, the growth was always sparse, and consisted of discrete, scattered colonies from which subcultures could easily be made.

Coverslip films were then made from the abundant growth in No. 1 tube, a loopful of organisms being obtained by drawing the loop along the whole length of the sloped surface of the serum. These film preparations were then stained by carbolic methylene blue (thoroughly matured) and by Neisser's method, and examined microscopically, using the $\frac{1}{12}$ in. oil immersion objective. At the commencement of the work we also examined film preparations made direct from the swab and

stained by similar methods. We soon, however, discontinued this form of examination, for, like preparations direct from swabbings of suspected diphtherial throats, the results obtained were by no means commensurate with the trouble and labour involved. In the Neisser-stained preparations the films were exposed to the action respectively of the acid methylene-blue solution and the bismark-brown solution for considerably longer periods than the few seconds originally suggested. This prolongation of the staining process was early recognised as necessary by Neisser himself, and has been generally adopted in this country. Beaton, Caiger and Pakes,⁵ in a paper dealing with the examination of throat material, have suggested a two minutes' immersion in each staining fluid, and this was the modification of the original method we employed in our work.

The detection, when present, of bacilli belonging to the diphtheria group, in which we include *B. diphtheriæ* (Klebs-Löffler bacillus), *B. xerosis*, *B. Hoffmanni*, *B. segmentosus coryzæ* and other unnamed but allied species, by microscopical examination presented but little difficulty in that the writers have had considerable experience in the microscopical examination of cultivations from swabbings taken from cases of suspected diphtheria—an experience, in the case of one of us, extending to over 20,000 such examinations during a period of more than ten years.

The organisms detected microscopically were further differentiated into Klebs-Löffler bacilli, Hoffmann's bacilli, and diphtheroids (that is, some one or other of the remaining members of the group), and the complete diagnosis recorded. In only one instance has it been found necessary, after fully working out the life-history of the bacillus in question, to alter the diagnosis first made. The one exception relates to the bacillus isolated from the throat of Steward, and which, after a complete study, was found to be identical with the non-pathogenic diphtheroid bacillus isolated from a specimen of cows' milk some years ago by one of the present writers.⁶

And we may here remark that the differential diagnosis of these diphtheroid bacilli was invariably made on the result of

the examination of the methylene-blue stained specimen derived from the blood-serum cultivation, as we are of opinion that the Neisser-stained specimens afford no information beyond that given more obviously and conclusively by the methylene-blue preparation. The value of Neisser's stain, moreover, is detracted from by the fact that quite 50 per cent. of the strains of diphtheroid bacilli other than the true diphtheria bacillus will, when examined under the conditions laid down as to age, medium, &c., show polar granules identical in appearance and situation with those originally considered as pathognomonic of the Klebs-Löffler bacillus (see also Table VII.).

Then, too, the streptococcus longus—a common inhabitant of the throat—and especially that rapidly-dividing form often met with, and dignified by some observers by the title “bacillary” form, will occasionally give appearances indistinguishable from those presented by the Klebs-Löffler bacillus, and these examples might easily be multiplied. On the other hand, species of *B. diphtheriæ* are often met with which, although typical as to morphology, cultural characters, bio-chemical reactions, and pathogenesis, fail to show the “Neisser's stain,” even in the culture first obtained from the human body. The application of Neisser's method as an aid to diagnosis has had a somewhat fictitious value attached to it as the result of the observations of Beaton, Caiger and Pakes,² already referred to, in that they used this method only, and their results were not controlled by a competent observer working only with methylene-blue stained specimens, except in forty of their cases, and further, that all the cases examined were cases admitted to the hospital and under treatment there for diphtheria. Again, we are inclined to think that many of the twenty-five cases recorded as diphtheria clinically, but in which they were unable to detect *B. diphtheriæ* by the aid of Neisser's method, would probably have given positive results if “methylene-blue” specimens had been prepared as well. This opinion is based on the results obtained in the Bacteriological Department of Guy's Hospital, which show that fully 20 per cent. of the stains of true *B. diphtheriæ* do not give

a positive result with Neisser's method, although typical culturally and in point of virulence.

Mervyn Gordon,⁹ too, lays great stress on the differential value of the Neisser staining of bacilli isolated from the throat; but the observations on which he bases his conclusions are too few to need any comment.

Next, in those cases where a diphtheroid organism was recognised an attempt was made to isolate it. Occasionally our efforts in this direction failed owing to the small number of this organism, and the enormous number of other organisms present in the specimens. In those cases where no diphtheroid organisms could be detected after examining numerous methylene-blue films in this way from the first tube of the series, the second tube was subjected to the same process.

Whenever a diphtheroid organism was detected microscopically in the films, a careful search was made in the second and third tubes—where the growth was naturally less profuse—for isolated colonies, or for spots where the diphtheroid organism was relatively abundant. Occasionally a pure colony was found; when this happened it was transferred to a fresh serum tube and a pure culture thus obtained. In other cases the organism sought was so mixed up with others that it was necessary to use plate cultivations in order to obtain a pure culture, and for this purpose the following method was adopted: A loopful from the most likely spot on the serum tube cultivation (as tested microscopically) was emulsified in 5 c.cm. of sterile broth, and two or three loopfuls of this emulsion were then rubbed over the surface of a "serum" plate (that is, about 15 c.cm. bullock's serum, inspissated at 80° C. in an ordinary petri dish) by means of the short arm of a previously sterilised L-shaped glass rod. Without recharging or further sterilising, this rod was immediately rubbed over the surface of a second and then a third plate. The few organisms adhering to the rod after rubbing the loopful of broth over the surface of the first plate were thus deposited on these latter plates, and after incubation in the ordinary way, usually yielded a scanty growth of discrete colonies

among which pure colonies of the diphtheroid organisms were sought.

Pure cultures having been obtained by one or other of the methods described above, the bacilli thus isolated were fully studied in parallel series with authenticated controls of the three chief members of the diphtheria group—namely, *B. diphtheria* (two varieties), *B. Hoffmanni* and *B. xerosis*—as to their (1) morphological characters; (2) staining reactions; (3) cultural appearances and chemical activities; and (4) pathogenesis, and their identity finally established after a careful consideration of all these points.

With regard to the first of these—the morphological appearances—we have already expressed the opinion that these are sufficiently characteristic to warrant a correct diagnosis in the majority of cases if specimens are prepared from eighteen-hour-old blood serum cultivations and stained with thoroughly matured carbolic methylene-blue. At the same time we sought further confirmation from the examination of microscopical preparations made from cultivations upon other media. Of such preparations, those made from cultures on alkaline potato incubated for thirty hours at 37° C. were undoubtedly the most helpful; for on this medium the presence of enormous clubbed forms,¹⁵ either evenly or faintly stained, or showing bars of deeply-stained protoplasm, readily differentiates the true diphtheria bacillus from the bacillus of Hoffman and other members of the diphtheria group whose growth on this medium is characterised by oval and spherical involution forms and coccoid bodies—clubbed and segmented forms, except small and ill-defined ones, being conspicuous only by their absence. The xerosis bacillus, be it noted, shows but a very scanty growth on alkaline potato, and even this scanty growth soon dies out.⁷

The recent observations of Abbott and Gildersleeve¹ on the occasional branching of the *B. diphtheria* as distinguished from the non-pathogenic members of the group, led us to hope that some assistance might be gained by studying the morphology of the bacilli we had isolated when cultivated for eight hours at 37° C. upon acid (+ 30) egg medium. In this hope, however, we were

disappointed, as we were unable to obtain branched forms in any of the cultivations—not even in our control cultures prepared with virulent strains of *B. diphtheriæ*.

Finally, in some cases in which we failed to detect a diphtheroid bacillus, one and often more fresh swabbings were made and examined as thoroughly as in the first instance.

(b) *Material obtained Post-mortem.*—At the *post-mortem* inspection of the bodies of general paralytics, some, and often all, the material detailed below was collected for examination, and generally in the order there given. The methods of examining the cultures prepared from this material corresponded exactly with those already described. In the event of a culture failing to develop a growth, the period of observation was extended from eighteen hours to seven days before recording the result as sterile.

(1) *Cerebro-spinal Fluid.*—The skin of the dorsum over the lumbar vertebræ was seared with a red-hot cautery iron, and as much cerebro-spinal fluid as possible (up to 5 cubic centimetres) was drawn off by means of "lumbar puncture" into a sterile syringe. The syringe was then detached from the needle and the cerebro-spinal fluid transferred to a sterile test tube. The fluid was first reinforced by incubating at 37° C. for twelve to eighteen hours, then thoroughly centrifugalised, and cultivations prepared upon inspissated blood serum, nutrient agar, and in broth from the centrifugalised deposit, after a preliminary microscopical examination.

(2) *Swabbings from the Pharynx.*—These were obtained and examined in a manner precisely identical with the swabbings collected from the fauces during life.

(3) *Heart Blood.*—As soon as the thorax was opened an incision was made in the pericardium and the surface of the right ventricle, or occasionally the right auricle, laid bare. This surface was then seared with the cautery iron, and the point of a sterile Pasteur pipette thrust through the seared area into the heart cavity, and a small quantity of blood (2 to 3 cubic centimetres) aspirated into the pipette. From the blood so collected

cultivations were established in broth, and on agar, and inspissated blood serum.

(4) *Swabbings from Bronchi*.—The lungs were removed from the body and separated from the heart. A section across one or other lung, often both, was then made at a convenient spot, and a swab, such as was employed in the collection of material from the throat, was passed into an open bronchus (avoiding contact with the cut surface of the lung) and pushed onwards, gently rotating it meanwhile, as far as it would go. It was then carefully withdrawn, returned to its sterile tube, and the latter labelled. The further steps of the examination were precisely as described for material from the throat and pharynx.

(5) *Bile*.—When the abdominal cavity was opened the gall bladder was sought for and drawn forward from under the edge of the liver. The exposed surface of the bladder was seared with the cautery iron, the point of a sterile Pasteur pipette thrust into the bladder through the seared area, and a few cubic centimetres of bile aspirated into the pipette. After collection, the examination of the material was proceeded with as described under heart blood.

(6) *Scrapings from the mucous membrane of the intestine*.—The apparatus used for collecting the material consisted of a small tin scoop mounted in an ordinary cork. This cork was used to close the mouth of a test tube in such a manner that the scoop was enclosed in the tube. The whole piece of apparatus was then prepared for use by sterilising in the hot-air oven for half an hour at 150° C.

The cæcum was found and drawn forward, the peritoneal surface of the intestine just above the cæcum seared with the cautery iron, and an incision made through the walls of the intestine within the seared area by means of a sterile knife. The cork, with its attached scoop, was removed from a test tube, the scoop passed into the cavity of the bowel through the incision in the intestinal wall, and the mucous membrane thoroughly scraped. The scoop was then removed, and, with the material scraped from the bowel in its bowl, replaced in the tube.

Scrapings from other portions of the intestinal canal were made in a similar manner.

Cultivations were established directly from the scrapings upon inspissated blood serum and agar, by means of a platinum loop.

Results Obtained from Examinations of the Throat during Life.

The number of cases examined totalled up to 138, and comprised 60 cases of general paralysis of the insane and 78 cases of other forms of insanity. Of these cases, Colney Hatch Asylum provided 88, 49 general paralysis and 39 other forms of insanity; and Claybury Asylum 50 cases, made up of 11 cases of general paralysis and 39 other forms of insanity, as shown in Table II.:—

TABLE II.
SOURCE AND CONDITION OF THE PATIENTS EXAMINED.

Asylum.	General paralysis of the insane.	Other forms of insanity.	Total all forms of insanity.
Colney Hatch	49	39	88
Claybury	11	39	50
Total	60	78	138

Of these 138 cases, 24 gave positive results—that is, we were able to detect the presence of a diphtheroid organism in 24 of this total, or 17·3 per cent. Unfortunately, owing to a variety of causes, we were able to isolate the organism from 15 only of these positive cases; in the remaining 9 cases the differential diagnosis between *B. diphtheria* and other members of the diphtheria group had to be based upon microscopical appearances alone. Even in these cases, however, we believe—for the reasons previously given—the margin of error to be extremely small. Assuming our results to be correct, we noted the presence of the *B. diphtheria* in 7 of these 24 positive cases (or 5·07 per cent.), the “diphtheroids” present in the remaining 17 cases being

B. Hoffmanni 14 times, *B. xerosis* twice, and an unnamed pigmented species once.

Tables III., IV., V. and VI. give the results we obtained dissected and tabulated to show:—(1) The incidence of diphtheroid organisms in the throats of the insane. (2) The incidence of *B. diphtheriæ* in the throats of the insane. (3) The incidence of *B. Hoffmanni* in the throats of the insane. (4) The incidence of diphtheroid organisms (excluding *B. diphtheriæ* and *B. Hoffmanni*) in the throats of the insane.

TABLE III.

SHOWING THE OCCURRENCE OF DIPHTHEROID ORGANISMS IN THE THROATS OF THE INSANE.

Source.	Cases of G.P.I. examined.	Diphtheroid organisms found.	Percentage incidence.	Cases of insanity other than general paralysis examined.	Diphtheroid organisms found.	Percentage incidence.
Colney Hatch ...	49	9	18·3	39	9	23·0
Claybury ...	11	1	9·0	39	5	12·8
Total ...	60	10	16·6	78	14	17·9

TABLE IV.

SHOWING THE OCCURRENCE OF *B. diphtheriæ* IN THE THROATS OF THE INSANE.

Source.	Cases of G.P.I. examined.	<i>B. diphtheriæ</i> found.	Percentage incidence.	Cases of insanity other than general paralysis examined.	<i>B. diphtheriæ</i> found.	Percentage incidence.
Colney Hatch ...	49	2	4·08	39	2	5·1
Claybury ...	11	1	9·00	39	2	5·1
Total ...	60	3	5·00	78	4	5·1

TABLE V.

SHOWING THE OCCURRENCE OF *B. Hoffmanni* IN THE THROATS
OF THE INSANE.

Source.	Cases of G.P.I. examined.	<i>B.</i> <i>Hoffmanni</i> found.	Per- centage incidence.	Cases of insanity other than general paralysis examined.	<i>B.</i> <i>Hoffmanni</i> found.	Per- centage incidence.
Colney Hatch ...	49	5	10·2	39	6	15·3
Claybury ...	11	0	0	39	3	5·1
Total ...	60	5	8·3	78	9	11·5

TABLE VI.

SHOWING THE INCIDENCE OF DIPHTHEROIDS (EXCLUDING *B. Diphtherie*
AND *B. Hoffmanni*) IN THE THROATS OF THE INSANE.

Source.	Cases of G.P.I. examined.	Diph- theroids found.	Per- centage incidence.	Cases of insanity other than general paralysis examined.	Diph- theroids found.	Per- centage incidence.
Colney Hatch ...	49	49	4·08	39	1	2·5
Claybury ...	11	11	—	39	0	—
Total ...	60	60	3·3	78	1	1·2

TABLE VII.

SHOWING THE IDENTITY OF THE DIPHTHEROID ORGANISMS OBSERVED.

Asylum.	Name.	Mental condition.	Methylene-blue preparation—diagnosis.	Neisser preparation, positive or negative.
Colney Hatch ..	Abbott ...	—	<i>B. Hoffmanni</i> ...	+
" ...	Abrams ...	—	<i>B. diphtheriæ</i> ...	+
" ...	Baker ...	G.P.I. ...	<i>B. Hoffmanni</i> ...	—
" ...	Denny ...	" ...	" ...	+
" ...	Galgaard ...	" ...	<i>B. xerosis</i> ...	+
" ...	Haszell ...	—	<i>B. Hoffmanni</i> ...	±
" ...	Hollinghurst ...	—	" ...	—
" ...	Kirkby ...	—	" ...	—
" ...	Leahay ...	—	<i>B. xerosis</i> ...	±
" ...	Moore ...	—	<i>B. Hoffmanni</i> ...	—
" ...	Rummary ...	—	<i>B. diphtheriæ</i> ...	—
" ...	Smith ...	—	<i>B. Hoffmanni</i> ...	—
" ...	Solomons ...	G.P.I. ...	" ...	+
" ...	Steward ...	" ...	<i>B. diphtheriæ</i> * ...	+
" ...	Taylor ...	—	" ...	+
" ...	Vail ...	G.P.I. ...	<i>B. Hoffmanni</i> ...	—
" ...	Wright, R. ...	" ...	<i>B. diphtheriæ</i> ...	+
" ...	Wright, W. ...	" ...	<i>B. Hoffmanni</i> ...	—
Claybury ...	8 ...	" ...	<i>B. diphtheriæ</i> ...	+
" ...	23 ...	—	" ...	+
" ...	45 ...	—	" ...	+
" ...	46 ...	—	<i>B. Hoffmanni</i> ...	—
" ...	49 ...	—	" ...	—
" ...	50 ...	—	" ...	—

* This organism eventually proved not to be *B. diphtheriæ* (v. Tables X. and XI.).

In Table VII. we have shown the particular patients, together with the mental condition of each, from whose throats we have isolated "diphtheroid" organisms, divided into two sections according to the asylum from which they were derived. The further particulars given refer to the differential diagnosis of the organisms, based on the result of the microscopical examination of methylene-blue stained specimens, and show also the result of the examination of Neisser stained preparations, the sign + indicating that polar granules, indistinguishable from those characteristic of the *B. diphtheriæ*, are present (see Neisser); the sign — indicating that polar granules are absent: whilst the sign ± indicates the presence of atypical granules.

Results Obtained from the Examination of Post-mortem Material.

The total number of cases examined *post-mortem* in this connection amounted to 86. These were all derived from the London County Asylum at Colney Hatch, and comprised 10 cases of general paralysis of the insane and 26 cases of other forms of insanity. Of these, 4 of the cases of general paralysis yielded evidence of the presence of diphtheroid organisms in the respiratory tract, but only one showed evidence of any general, and that probably terminal, infection, or even *post-mortem* invasion, by *B. Hoffmanni*. This organism was quite typical in its cultural reactions, and was totally devoid of virulence or toxicity. Of the remaining 5 cases, 1 (W. W.), whose throat had been examined about a month before death with positive results, failed to give any evidence *post-mortem* of the presence of diphtheroid organisms within the body. Of the 25 cases of forms of insanity other than general paralysis, 4 gave evidence of the presence of diphtheroid organisms in the respiratory tract, none of general infection.

TABLE VIII.

SHOWING THE OCCURRENCE OF DIPHTHEROID ORGANISMS IN POST-MORTEM MATERIAL.

—	Number of cases examined.	Diphtheroid bacilli found in the respiratory tract.	Per-centage.	Diphtheroid bacilli found in other situation as well.	<i>B. diphtheria</i> found in any situation.
General paralysis of the insane	10	4	40·0	1	0
Cases of insanity other than general paralysis of the insane	26	4	15·3	0	0

The full details of the *post-mortem* material examined from the ten cases of general paralysis, and the results obtained, are shown in tabular form in Table IX.

In Tables X. and XI. are given the chief characters of the strains of diphtheroid bacilli which were isolated during the course of this investigation, contrasted with authentic stock cultivations of *B. diphtheriæ*, *B. Hoffmanni*, and *B. xerosis*. Finally, the pathogenicity of most of the diphtheroid bacilli we had isolated was tested in the following manner, premising that these and all the other animal experiments performed in connection with this investigation were carried out in the Bacteriological Laboratory of Guy's Hospital:—

Experiment 1.—One loopful (about 2 mg.) of a forty-eight-hour-old blood serum culture was emulsified in 1 c.cm. sterile broth and injected into the subcutaneous tissue of the abdomen of a small (250 gram.) guinea-pig.

Experiment 2.—A similar dose was injected into a second guinea-pig and immediately followed by the introduction of 500 units of antidiphtheritic serum.

None of the guinea-pigs showed any ill-effects, either local or general, as the result of the inoculations.

Note.—Four of the animals used in these experiments died during the third week after inoculation, at which time peat moss litter was substituted for hay in their cages. *Post-mortem* no evidence of infection by *B. diphtheriæ* could be detected. The intestines were enormously distended with macerated peat moss, and were ruptured in many places, the peat moss being found in the peritoneal cavity.

Experiment 3.—Possible toxine production was tested by filtering a three-day-old broth culture through a porcelain candle, and injecting 5 c.cm. of the filtrate so obtained into a guinea-pig of about 200 grammes weight.

The animals so treated showed no symptoms whatever. Control animals inoculated under identical conditions with cultivations of true *B. diphtheriæ* (strains "Powys" and "Wood") and toxins obtained therefrom gave positive results.

Bearing in mind the possibility that the organisms isolated from the throats of the insane might be *B. diphtheriæ* of extremely low virulence, a further set of inoculations was carried out—employing for the purpose five strains of bacilli,

diagnosed microscopically as true Klebs-Löffler bacilli, two of *B. Hoffmanni*, and one of *B. xerosis*, as follows:—

Experiment 4.—Three cubic centimetres of a forty-eight hour-old broth cultivation were injected subcutaneously into the abdominal parietes of a guinea-pig of about 250 grammes weight.

Control animals were inoculated with 1 cubic centimetre of similar cultivations derived from strains "Powys" and "Wood" respectively (Table XIV.).

The result of this experiment was that the animals inoculated with cultures from "Abrams" and "8" died at seventy-two and forty-eight hours respectively, the necropsies affording typical pictures of the death from infection by *B. diphtheriæ*. None of the other animals were affected.

The two control animals died within twenty-four hours.

From these experiments it is clear that two of the strains of *B. diphtheriæ* isolated during our investigations were virulent, although the virulence, as indicated by the large dose required and the length of time that elapsed before death, was distinctly lowered, whilst the remaining three strains were, so far as we were able to judge, avirulent.

CONCLUSIONS.

As the results of our observations we would formulate the following conclusions:—

(1) That the percentage incidence of all "diphtheroid" organisms in the throats of the insane (17·3 per cent.) is not in excess of that noted in the sane population (18·5 per cent.) outside the walls of an asylum.

(2) That the percentage incidence of genuine *B. diphtheriæ* (5·07 per cent.) in the throats of the insane is smaller still (a large proportion of the diphtheroid organisms noted were common saprophytic members of the diphtheria group of bacilli), and compares well with 6·9 per cent. in the healthy sane.

(3) That there is no evidence to show that *B. diphtheriæ* is more common in the throats of general paralytics (5 per cent.)

than in the throats of cases of other forms of insanity (5.1 per cent.).

(4) That the number of general paralytics examined *post-mortem* is too small to enable any definite conclusions to be drawn therefrom. At the same time, it is a significant fact the *B. diphtheriæ* was not isolated from any of these cases.

(5) That the majority of the strains of *B. diphtheriæ* isolated from the throats of the insane are of low virulence and slight toxicity, and so compare in these respects with the types found occasionally in the throats of the healthy sane.

(6) That having due regard to the above conclusions, we are unable to trace any causal connection between *B. diphtheriæ* and general paralysis of the insane.

TABLE IX.
RESULTS OF EXAMINATION OF *post-mortem* MATERIAL FROM GENERAL PARALYTICS.

Source.	Name.	DIPHTHEROID ORGANISMS NOTED.			ORGANISMS ISOLATED FROM—				
		Swabbing of tonsils during life.	Swabbing of pharynx.	Swabbing of bronchus.	Cerebro-spinal fluid.	Heart blood.	Bile.	Scraping from intestinal mucosa.	
1	C. B., October 30, 1903 ...	0	+	+	Sterile ...	(<i>B. coli</i>) ...	Sterile ...	—	
2	M. G., December 8, 1903 ...	0	+	—	" ...	Sterile 0	(<i>B. coli</i>) ...	—	
3	R. B., December 7, 1903 ...	+	0	—	(<i>Staphylococcus aureus</i>)	0	(<i>B. coli</i>)	—	
4	G. C., September 28, 1903	0	0	—	(<i>S. albus and aureus</i>)	0	Sterile	{ (1) Colon (2) Cecum (3) Ileum }	
5	J. F., November 9, 1903 ...	0	—	—	Sterile ...	(<i>B. coli</i>)	"	—	
6	E. H., January 25, 1904 ...	0	—	—	(<i>S. aureus</i>)	(<i>S. aureus</i>)	"	—	
7	R. L., January 18, 1904 ...	0	—	—	(<i>S. albus</i>)	Sterile	"	—	
8	J. S., November 23, 1903 ...	+	+	+	0	(<i>B. coli</i>)	(<i>B. coli</i>)	—	
9	G. H. V., October 6, 1903 ...	+	+	—	<i>B. coli</i> ...	(<i>B. Hoffmanni</i>)	Sterile	(<i>B. Hoffmanni</i>)	
10	W. W., December 12, 1903	+	—	—	(<i>S. aureus</i>)	Sterile 0	0	—	

+ Indicates the isolation of a diphtheroid organism.

— Indicates a negative result so far as concerns diphtheroid organisms.

0 Signifies that this material was not examined.

TABLE X.—MORPHOLOGY AND STAINING REACTIONS OF DIPHTHEROID ORGANISMS ISOLATED.

Name or Designation of bacillus.	Source.	Morphology on blood serum after 12-18 hours' incubation at 37° C. and stained carbolic methylene blue.	"Gram" staining.	"Neisser" staining.	Branching on acid egg media at 8 hours.	Morphology on alkaline potato after 24 hours at 37° C., and stained carbolic methylene blue.	Diagnosis.	Mental condition of patient.
Controls	<i>B. diphtheriae</i> (Powys)	Discharge from case of diphtheritic rhinitis.		—	Nil.	Large involution forms, showing marked clubbing and segmentation of protoplasm, and exhibiting meta-chromatism.	<i>B. diphtheriae</i> ...	Sane.
	<i>B. diphtheriae</i> (Wood)	Discharge from ear in case of faucial diphtheria.	+	+	"	Ditto ...	<i>B. diphtheriae</i> , var. sheath	"
	<i>B. Hoffmanni</i>	Laboratory stock. Originally isolated from discharge of post-diphtheritic rhinorrhea.	+	—	"	Short bacilli and coccoid bodies, some slightly pear-shaped. No clubbed or large barred forms.	<i>B. Hoffmanni</i> ...	"
	<i>B. xerosis</i>	Laboratory stock. Originally isolated from normal conjunctival sac.	+	+	"	As <i>B. Hoffmanni</i> , above.	<i>B. xerosis</i> ...	"

+ = positive result.

— = negative result.

± = positive but atypical result.

TABLE X.—continued.

Number	Name or Designation of bacillus.	Source.	Morphology on blood serum after 12-18 hours' incubation at 3° C. and stained carbolic methylene blue.	"Grain" staining.	"Neisser" staining.	Branching on acid egg media at 8 hours.	Morphology on alkaline peptone after 24 hours at 37° C. and stained carbolic methylene blue.	Diagnosis.	Mental condition of patient.
1	Abbott ...	Swabbing from pharynx.	As <i>B. Hoffmanni</i> ...	+	+	Nil.	As <i>B. Hoffmanni</i> ...	<i>B. Hoffmanni</i> ...	—
2	Abrams ...	"	" <i>B. diphteriae</i> ...	+	+	"	" <i>B. diphteriae</i> ...	<i>B. diphteriae</i> ...	—
3	Denny ...	"	" <i>B. Hoffmanni</i> ...	+	+	"	" <i>B. Hoffmanni</i> ...	<i>B. Hoffmanni</i> ...	G. P. I.
4	Galgaard ...	"	" <i>B. xerosis</i> ...	+	+	"	"	<i>B. xerosis</i> ...	"
5	Haszell ...	"	" <i>B. Hoffmanni</i> ...	+	+	"	"	<i>B. Hoffmanni</i> ...	—
6	Hollinghurst ...	"	" <i>B. diphteriae</i> ...	+	+	"	"	<i>B. xerosis</i> ...	—
7	Leahay ...	"	" <i>B. Hoffmanni</i> ...	+	±	"	"	<i>B. Hoffmanni</i> ...	—
8	Rummery ...	"	" <i>B. diphteriae</i> ...	+	—	"	" <i>B. diphteriae</i> ...	<i>B. diphteriae</i> ...	—
9	Steward ...	"	"	+	+	"	" <i>B. Hoffmanni</i> ...	"Diphtheroid 1" ...	G. P. I.
10	Taylor ...	"	"	+	—	"	" <i>B. diphteriae</i> ...	<i>B. diphteriae</i> ...	—
11	Vail ...	"	" <i>B. Hoffmanni</i> ...	+	—	"	" <i>B. Hoffmanni</i> ...	<i>B. Hoffmanni</i> ...	G. P. I.
12	Wright, R.	"	" <i>B. diphteriae</i> ...	+	+	"	" <i>B. diphteriae</i> ...	<i>B. diphteriae</i> ...	"
13	Wright, W.	"	" <i>B. Hoffmanni</i> ...	+	—	"	" <i>B. Hoffmanni</i> ...	<i>B. Hoffmanni</i> ...	"
14	8 ...	"	" <i>B. diphteriae</i> ...	+	+	"	" <i>B. diphteriae</i> ...	<i>B. diphteriae</i> ...	"
15	50 ...	"	" <i>B. Hoffmanni</i> ...	+	—	"	" <i>B. Hoffmanni</i> ...	<i>B. Hoffmanni</i> ...	—

+ = positive result.

— = negative result.

± = positive but atypical result.

TABLE XI.—BIOLOGICAL CHARACTERS OF DIPHTHEROID ORGANISMS ISOLATED.

Number.	Name or designation.	Blood-serum culture at 24 hours.	Agar streak culture at 24 hours.	Gelatine streak culture at 3 days.	Gelatine stab culture at 3 days.	Alkaline potato.	Glucose ferment broth culture Anaerobic at 24 hours.	Reaction.	Litmus milk culture at 3 days.	0.5 per cent. dextrose broth culture at 48 hours.	Lead broth culture for presence of H ₂ S.	Peptone water culture for presence of indol.	Pigment formation.	Nitrate broth for nitrates.
<i>Controls</i>														
(<i>B. diphteria</i> (Wood, Powys)	Small round pulvinate colonies, whitish or dirty-grey in colour, opaque, darker at centre, coarsely granular surface, entire margin.	Generally as on blood serum, but translucent; or continuous dull whitish layer showing discrete colonies at the margins.	As on agar, but distinctly scantier growth.	Line of small spherical colonies sloping to bottom of needle track.	Delicate, moist glistening layer, so-called "invisible" growth.	Flocculent or powdery growth deposited on sloping side of tube, or slipping to the bottom.	+	+	+	+	+	Nit.	+
	<i>B. Hoffmanni</i>	"	"	"	"	"	"	—	—	0	+	+	—	+
	<i>B. zerois</i> (sub-cultures)	As <i>B. diphteria</i> but drier and scaly.	"	Scanty growth as opalescent streak.	Scanty growth.	Very scanty "invisible" growth; bacillus soon dies on this medium.	"	—	—	—	+	+	—	+
1	Abbott ...	As <i>B. diphteria</i>	"	"	"	"	"	—	—	0	+	+	—	+
2	Abrams ...	"	"	"	"	"	"	—	—	0	+	+	—	+
3	Denny ...	"	"	"	"	"	"	+	+	0	+	+	—	+
4	Galgard ...	"	"	"	"	Dirty greyish layer, very limited in extent.	"	—	—	0	+	+	—	+

+ = acid reaction, or presence of substance tested for.

— = alkaline reaction, or absence of substance tested for.

± = faintly acid reaction, or traces of substance tested for.

0 = no change.

TABLE XI.—continued.

Number.	Name or designation.	Blood-serum culture at 24 hours.	Agar streak culture at 24 hours.	Gelatin streak culture at 3 days.	Gelatin stab culture at 3 days.	Alkaline potato.	Glucose for-mate broth culture. Anaerobic at 24 hours.	Litmus milk culture at 3 days.		Reaction at 48 hours.	Lead broth culture for H ₂ S.	Pepton water culture for indol.	Pigment formation.	Nitrate broth for presence of nitrites.
								Reac-tion.	Clot.					
5	Haszall ...	<i>As B. diphtheria</i>	Generally as on blood serum, but translucent; or con-tinuous dull whitish layer showing dis-crete colonies at the mar-gins.	Scanty growth as opalescent streak.	Scanty growth.	"Invisible" growth.	Flocculent or powdery deposited on sloping side of tube, or slipping to the bottom.	0	—	+	+	—	—	+
6	Hollinghurst	"	"	"	"	Very scanty ditto	"	0	—	0	+	—	—	+
7	Lehay ...	"	"	"	"	"Invisible" growth.	"	0	—	+	+	—	—	+
8	Rummary ...	<i>As B. diphtheria</i>	"	"	"	Moist, dull, yellow layer, soon becoming dry and powdery.	<i>As B. diphtheria</i> , but very scanty growth.	+	—	0	+	+	Yel-low	+
9	Steward ...	but yellowish colonies.	"	"	"	"Invisible" growth.	"	+	—	0	+	+	—	+
10	Taylor ...	<i>As B. diphtheria</i>	"	"	"	"	"	+	—	0	+	+	—	+
11	Vail	"	"	"	"	"	"	—	—	0	+	+	—	+
12	Wright, R. ...	"	"	"	"	"	"	—	—	0	+	+	—	+
13	Wright, W. ...	"	"	"	"	"	"	—	—	0	+	+	—	+
14	8 ...	"	"	"	"	"	"	—	—	0	+	+	—	+
15	50 ...	"	"	"	"	"	"	—	—	0	+	+	—	+

+ = acid reaction, or presence; of substance tested for.

— = alkaline reaction, or absence of substance tested for.

± = faintly acid reaction, or traces of substance tested for.

0 = no change.

TABLE XII.

SHOWING RESULT OF INOCULATION OF BACILLARY EMULSIONS.

Guinea-pig No.	Weight in grams.	Inoculated with "Diphtheroid" bacillus from.	Dose of diphtheria antitoxin L.I.P.M.	Date of inoculation.	Result.
1	140	Abbott ...	<i>Nil.</i>	Dec. 10, 1903	Unaffected.
2	130	" ...	500 units	"	"
3	200	Abrams ...	<i>Nil.</i>	"	Died Dec. 27, 1903.
4	200	" ...	500 units	"	Unaffected.
5	200	Haszell ...	<i>Nil.</i>	"	"
6	220	" ...	500 units	"	"
7	170	Hollinghurst ...	<i>Nil.</i>	"	Died Dec. 29, 1903.
8	220	" ...	500 units	"	Unaffected.
9	190	Leahay ...	<i>Nil.</i>	"	"
10	260	" ...	500 units	"	"
11	190	Rummery ...	<i>Nil.</i>	"	"
12	170	" ...	500 units	"	"
13	180	Taylor ...	<i>Nil.</i>	"	"
14	220	" ...	500 units	"	"
15	230	Steward ...	<i>Nil.</i>	"	Died Dec. 27, 1903.
16	210	" ...	500 units	"	"
17	200	Wright, R. ...	<i>Nil.</i>	"	"
18	250	" ...	500 units	"	"
19	190	Wright, W. ...	<i>Nil.</i>	"	"
20	230	" ...	500 units	"	Died Dec. 26, 1903.
21	150	Denny ...	<i>Nil.</i>	Dec. 11, 1903	Unaffected.
22	170	" ...	500 units	"	"
23	160	" 8 " ...	<i>Nil.</i>	Dec. 15, 1903	"
24	150	" ...	500 units	"	"
<i>Con trols.</i>					
25	180	Powys ...	<i>Nil.</i>	Dec. 10, 1903	Died Dec. 11, 1903.
26	220	" ...	500 units	"	Unaffected.

TABLE XIII.

SHOWING RESULT OF INOCULATION OF FILTERED CULTURES.

Guinea-pig No.	Weight in grams.	Inoculated with filtered cultures (? toxins) of diphtheroid bacilli from	Date of inoculation.	Result.
27	260	Abbott ...	Dec. 19, 1903	Unaffected.
28	210	Abrams ...	"	"
29	190	Denny ...	"	"
30	200	Hollinghurst ...	"	"
31	160	Leahay ...	"	"
32	270	Steward ...	"	"
33	210	Wright, W. ...	"	"
34	200	Wright, R. ...	Jan. 10, 1904	"
35	190	Haszell ...	"	"
36	220	Taylor ...	"	"
<i>Con trols.</i>				
37	220	Powys ...	"	Died Jan. 12, 1904.
38	200	Wood ...	"	"

TABLE XIV.

SHOWING EFFECT OF INOCULATING LARGE DOSES OF LIVING CULTIVATIONS.

Guinea-pig No.	Weight in grams.	Inoculated with diphtheroid bacilli from.	Organism diagnosed as	Dose of cultivation.	Date of inoculation.	Result.
				c.cm.		
39	300	Abbott ...	<i>B. Hoffmanni</i>	3	Jan. 12, 1904	Unaffected.
40	290	Abrams ...	<i>B. diphtheriae</i>	3	"	Died Jan. 15, 1904.
41	270	Haszall ...	<i>B. Hoffmanni</i>	3	"	Unaffected.
42	270	Leahay ...	<i>B. xerosis</i> ...	3	"	"
43	240	Wright, R.	<i>B. diphtheriae</i>	3	"	"
44	270	Rummery ..	"	3	"	"
45	290	Taylor ...	"	3	"	"
46	300	" 8" ...	"	3	"	Died Jan. 13, 1904.
Controls						
47	260	Powys ...	"	1	"	Died Jan. 14, 1904.
48	250	Wood ...	"	1	"	" "

Note.—Since the above observations were completed, fresh interest has been aroused in connection with the pathology of general paralysis of the insane by the views expressed by Dr. Ford Robertson in his Morrison Lectures delivered before the Royal College of Physicians of Edinburgh in January, 1906; for in these lectures he attributes the possession of specific pathogenetic properties to his *B. paralyticans*, and regards this organism as the causal agent in the production of general paralysis. As the grounds upon which these claims are based appear to the critical observer open to question, further observations on the rôle played by members of the diphtheria group of bacilli in the production of general paralysis are now being carried out in conjunction with J. P. Candler, M.A., M.B., D.P.H., Assistant Pathologist at the Pathological Laboratories of the London County asylums, the result of which will be recorded in a future communication.—J.E.

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138 *Diphtheroid Organisms in the Throats of the Insane.*

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MECHANICAL PRINCIPLES IN DENTISTRY.

Read before the Odontological Society of Great Britain

BY

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THE two particular parts of dental surgery I wish to touch upon are the condensation of cohesive gold and the extraction of teeth.

Different operators have different methods of condensing gold, and the comparative value of these methods has always been a matter of considerable interest. The simple experiment of bringing two pieces of well-annealed cohesive foil together, without pressure beyond that of the weight of one of them, shows that a good variety of gold coheres very readily, and that the force required to condense an ordinary filling is not needed so much to make the gold cohere, as to bend its layers into sufficiently close apposition for the natural cohesion to take place. All our methods of condensation are only so many ways of applying force to effect this apposition between the layers of gold.

In order to understand the effect of a force, certain data must be known concerning it. These are:—

- (1) The point of application of the force.
- (2) Its direction.
- (3) Its magnitude.
- (4) The time during which it is applied.

It is to variations in these data that we must look for the explanation of the differences between the various methods of condensation, just as differences of amount and duration of pressure account for differences of effect produced by blows given by the ram of a battleship and a shot from one of its guns, although the amount of kinetic energy may be the same in both cases. The methods of condensation most in use, and that we need consider, are those of hand pressure, the hand mallet, the automatic mallet, and the rapid-blow mallets, which last differ somewhat one from another.

The question of the *point of application* is a very simple one, as it is merely a matter of bending the plugger, or rather choosing one that is suitably bent, to bring its working face, which is the point of application of the condensing force, to any part of any cavity (Fig. 1).

When we come to the *direction* of the force we find that hand pressure is sharply marked off from all methods depending on the use of a mallet, by the fact that with hand pressure a suitable

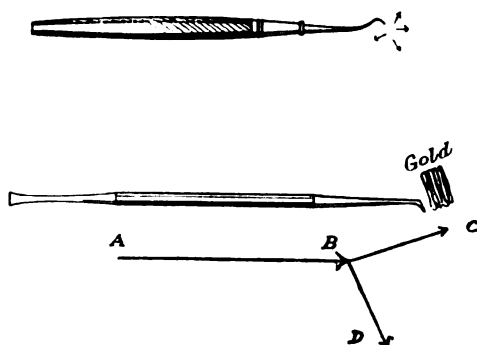


Fig. 1.

manipulation of the plugger shaft by the fingers will cause the point to exert a pressure in any direction whatever. This is very marked in the case of the useful spiral or screw pluggers.

In all kinds of malleting, on the other hand, the direction of the force exerted is limited by the direction of the blow given to

the plugger. Although limited *by* the direction of the blow, it is not correct to say that it is limited *to* that direction, because any single force can, by the ordinary rules of statics, be resolved into two or more that make acute angles with the direction of the original force. If, for instance, a plugger be held not vertical to the surface of the gold to be condensed, but inclined at an angle of say 30 degrees to the vertical, the mallet blow may be resolved into two forces, one acting vertically and going to condense the gold, the other acting parallel to the surface and either forcing the gold towards the cavity wall, or away from it, according to the direction of the original blow (Fig. 1).

A very important factor in condensation is the *magnitude* of the force exerted. It is obvious that whatever method is used the magnitude of the force can be varied at the will of the operator, from nothing at all, to the greatest the patient can conveniently bear, but on account of its very short duration the patient can put up with a greater actual pressure from a mallet than from a hand instrument.

It is well to remember, however, that although the patient may experience no inconvenience, the enamel edge is readily crumbled by a direct blow from a steel instrument.

With a given amount of pressure the condensing effect will vary with the area of the surface of the plugger point, and the angle that surface makes with the direction of the pressure. It has been pointed out by Dr. Miller that, other things being equal, the condensing effect of two pluggers will be in inverse ratio to the area of their working points. The reason of this is



Fig. 2.

that the condensing effect depends not on the total pressure but on the pressure per unit area ; so that the condensing effect of a certain pressure can be increased by diminishing the size of the plugger point (Fig 2), the limit to this increase being reached when the point becomes so small that it pierces the gold instead of

carrying the layers before it. Again, if the force, or in the case of mallets the long axis of the shaft, is not vertical to the surface of the gold, there is some loss of condensing effect, which in certain cases can be accurately determined. The convenience of using a plugger point whose striking face is not at right angles to its shaft is so great that it is well worth while to investigate what is the actual loss in ordinary cases.

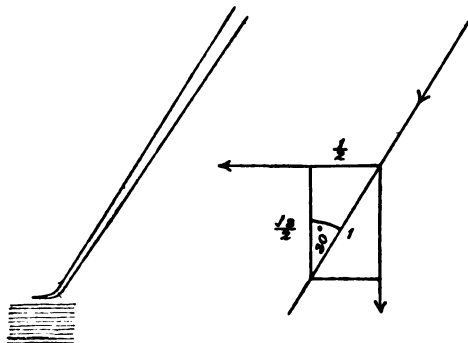


Fig. 3.

Imagine a plugger so constructed as to strike the gold in a direction inclined 30 degrees to the vertical (Fig. 3). Drawing lines parallel to—

- (1) The surface of the gold ;
- (2) Its normal ;
- (3) The shaft of the plugger ;

and completing the parallelogram so that its diagonal is parallel to the shaft, we shall have represented graphically the magnitudes of the force of the blow, the resultant vertical to the surface of the gold and available for condensation, and the resultant along the surface and not so available. If the force of the blow be taken as unity, the magnitude of its vertical component will be the cosine of the angle of 30°, which is rather more than $\frac{4}{5}$. So that the loss in this case is less than $\frac{1}{5}$ of the original blow, a quantity entirely negligible, compared with the convenience of such an arrangement.

In the more extreme instance of an angle of 45° (Fig. 4) the vertical force is cosine 45°, about $\frac{7}{10}$; here the loss is about $\frac{3}{10}$,

which again is hardly worth mentioning. We may, I think, conclude that with all ordinary shapes of pluggers the gain of convenience attained by bending the shaft far outweighs in importance the slight loss of power.

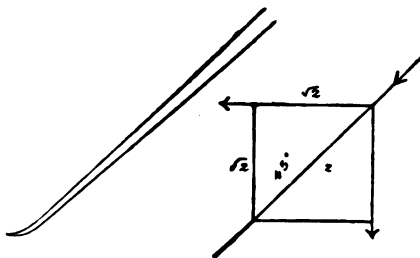


Fig. 4.

The last consideration is the *time* during which the force is applied, and this is of very great importance, because the layers of gold take a certain definite, although small, time to bend and come into apposition, particularly when a cylinder or pellet of considerable size is being condensed. If in this case the pressure is applied for only a very short time, as may happen if a rapid-blow mechanical mallet is used, the superficial layers may be condensed, but the pressure may have risen to its maximum and fallen again before there has been time for it to be transmitted to the deeper parts of the pellet. In other words, the blow in this particular case lacks penetration. From this point of view hand pressure stands easily first, as the pressure can be kept up for an indefinite time. It is the method almost invariably used when, as in noncohesive work, a great thickness of material has to be condensed at once.

Next to hand pressure, in point of penetration, I think we may place the hand mallet. With this instrument the large plugger handle, with its considerable inertia, the heavy, soft and usually lead-faced mallet, moving with a low velocity, combine to keep the pressure up for a longer time than would be the case with the mechanical mallets, and we all know that some magnificent work is done with this instrument.

Next may be placed the automatic mallet, still with a heavy shaft but a lighter hammer, made not of lead but of unyielding iron, and driven with a greater velocity; on the whole, giving a less penetrating blow, that is, keeping the pressure at a maximum for a shorter time than the hand mallet.

Still less weight and greater speed of striking mechanism are the characteristics of the rapid-blow mallets, as represented by the electro-magnetic, the Bonwill mechanical, and the Power, with its modifications (Fig. 5).

In the electro-magnetic and the Bonwill engine mallets the plugger with its handle has much greater weight, and consequently inertia, than in mallets of the power class, some of which, perhaps, represent the extreme type of rapid-blow mallets, as in them the weight of the actual part which strikes the gold is reduced to a minimum.

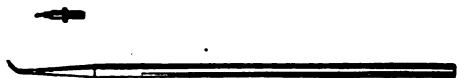


Fig. 5.—Striking parts of Bonwill and Power's angle mallets.

The general conclusion one comes to with regard to the rapid-blow mallets is, that although not so well suited for thick pellets, they are quite unrivalled for efficiently and speedily condensing heavy rolled foil; in fact, one may go further and say that by far the most rapid way of building a dense and strong contour filling is to lay on No. 40 or 60 foil, layer by layer, with a rapid-blow mallet.

I will now pass on to the question of extraction of teeth.

This differs much from most of the other operations of surgery, as the tissues concerned have very different degrees of hardness, the tooth being a rigid body surrounded by material of a relatively yielding nature.

This condition determines much of the technique of the operation of extraction, and at the same time renders the discussion of the problem an easy matter.

Let me say that I am not going to presume to teach members how to take out teeth, but will say a few words on the subject of the extraction instruments considered as examples of the so-called simple machines or mechanical powers. Of these the elevators are the more simple in construction (Fig. 6).

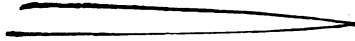


Fig. 6.

Apart from being used with a mere pushing action which calls for no further consideration, an elevator may be used on the principle of *the wedge*, the *simple lever*, and the *wheel and axle*.

The *wedge* action may either be used alone or form an unavoidable preliminary to some other movement. In fact, it quite often happens, in using an elevator or pair of forceps, that by the time the blade is applied in its proper position, the root is already loosened by the wedge action brought into play.

The power that may be applied by a blade used as a wedge is considerable, the mechanical advantage being measured by the cosecant of the angle at the point of the wedge; in the case of the ordinary straight elevator the power might be multiplied some five or six times.

The straight elevator may also be used as a simple lever, but, although the mechanical advantage is great, this method of employment is seldom of much use, as it is rarely possible to find a fulcrum and point of application in such positions that the force is exerted in any useful direction. An illustration of the amount of the power and its unfavourable direction is found in the classical case of the fracturing of the maxillary tuberosity during extraction of upper third molar with the straight elevator.

Either straight or curved elevators may be used with great advantage on the principle of the wheel and axle.

In this case the power is applied to the instrument by rotation of the handle on its long axis.

In the straight elevator the point of application of the force is the sharp edge of the blade a little way behind its point; in the

curved form it is at the end of the curved portion, the principle in both cases being exactly the same. The handle is, or should be, of sufficient size and such a shape as to be easily grasped by the hand without wasting power that is required for rotation, and in all cases the power is the same, namely, the pronation or supination of the forearm.

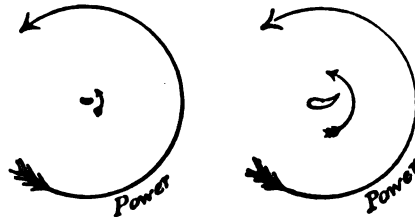


Fig. 7.—Diagrams of straight and curved elevators.

The power being the same, the comparative mechanical advantage of different elevators will be inversely proportional to the distance of the point of application of the force from the axis of rotation (Fig. 7).

In the straight instrument this distance is not very different from the width of the blade; in the curved one it corresponds to the length of the curved portion.

Used in this way the straight elevator has the advantages of taking up but little room, and exerting a great force in an upward direction, with only a small range of motion, for which reasons it is the favourite instrument with many operators for the extraction of lower third molars.

A pair of forceps is a more complicated instrument than an elevator, but if it is firmly holding a tooth its action is in principle a very simple one. In fact, as tooth and forceps form together one rigid bar, the forceps can hardly be said to act as one of the machines at all, but must rather be looked upon as an extension or handle to the tooth, in much the same way as a spanner forms a temporary handle to a nut. Mechanically, the chief interest lies in maintenance of the hold on the root.

The simplest case to take is that of a pair of straight forceps applied to an upper front tooth, the long axis of the root being in the same straight line as that of the forceps.

We will imagine that an attempt is made to loosen the root by a labial dislocation, and that the root is sufficiently solid not to crush during the operation.

There is immediately a tendency for the axis of the forceps to be inclined away from the direction of the axis of the root, just as if an attempt were made to wrench the root sideways in such a way as to force the blades of the forceps open.

This force, tending to loosen the hold, is proportional to the power applied to the forceps, and is entirely independent of the instrument or the position of its joint.

This tendency for the blade to open is, of course, counteracted by the operator's grip of the handles, but the efficiency of the

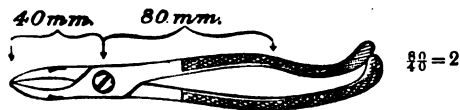


Fig. 8.

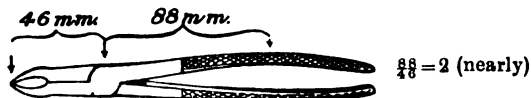


Fig. 9.—Mechanical advantage of various forceps.

grip to maintain the blades in close apposition to the root depends on the mechanical advantage of the particular pair of forceps used, being greater or less according as the joint is nearer to the tips of the blades or further away from them (Figs. 8 and 9).

The mechanical advantage of a pair of forceps is measured by a fraction, the numerator of which is the number of units of length from the joint to the point where the hand grip is applied, and the denominator the length from the joint to the tips of the blades.

This question of mechanical advantage is of considerable importance, because in cases where the root offers much resistance the force tending to open the blades is very great, and unless the forceps are of a type possessing great mechanical advantage, the operator's strength is chiefly taken up in efforts to keep hold of the root, and he has very little left for the proper motion of extraction.

This we found to our cost in our student days when we attempted to extract a firmly implanted upper molar with a pair of long-bladed "bayonets," instead of the short and stout-bladed, though, perhaps, less convenient full molar forceps.

In cases where the root is broken down, and perhaps dome-shaped, we find that the attempt at outward dislocation may not open the blades, but cause the inner one to tend to slide off the root and describe an arc with the point of the outer blade as a centre.

This annoying tendency is not counteracted by approximating the handles, as the more the blades close the worse is the hold on the root. It is rather met by a strong pressure towards the apex of the root during the whole of the loosening process. A part of this pressure is transmitted to the blade that is tending to slip, counteracting this tendency and keeping it in equilibrium until the dislocation is accomplished.

THE RELATION OF THE KIDNEYS TO METABOLISM.

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THE effects following on the removal of large portions of the kidneys of dogs were studied by Rose Bradford in 1892. In the first place, he found that animals deprived of three-quarters or more of their total kidney weight rapidly wasted, and died in two or three weeks, or even less; and, although they often refused food, they passed daily an amount of urea almost or quite equal to that passed by the same animals on full diet before operation. Secondly, he observed that after the removal of a portion of one kidney, the urine became more abundant and more dilute, and the dogs were apparently unable to excrete a concentrated urine; this effect was intensified by the subsequent removal of the opposite kidney. Bradford concluded that the kidneys in some manner normally control the nitrogenous metabolism, and that in the absence of sufficient kidney substance this metabolism becomes excessive.

In view of their extreme importance, a repetition of these experiments appeared advisable; it was hoped, too, that more

complete analyses of the urine might throw some light on the course of nitrogenous metabolism as a whole. This paper contains a preliminary account of our observations.

METHODS.

Cats were used for these experiments. They were anæsthetised with chloroform and ether, the anæsthesia being maintained by ether throughout the operation.

The abdomen was opened in the middle line, and the kidney drawn up into the wound; the capsule was opened, and stripped off the kidney. The renal vessels were digitally compressed, a wedge cut out of the kidney, and the cut surfaces brought into apposition and kept together by two or three sutures passing deeply through the kidney substance. The kidney was then replaced in its capsule and the latter was closed by a continuous suture; the kidney was returned to its place and the abdominal wound closed. No vessels were ligatured, since forceps are so apt to damage the kidney substance: a little blood collects between the kidney and capsule, where it clots and checks further loss of blood.

Two or three weeks later the opposite kidney was removed under ether anæsthesia through an abdominal incision.

The animals were kept in cages whose floor consisted of a wire netting; the cages stood upon a zinc plate, sloping towards the centre, which was perforated by a small hole. The urine ran down the zinc sheet through the hole into a basin containing a little chloroform. The urine and fæces were collected every twenty-four hours, and very great care was taken to keep the urine free from food or fæces.

The cats were kept at a fairly even, moderate temperature, and were allowed some exercise daily in the laboratory.

The food was measured daily, and any food left over was also measured. Their diet consisted of minced meat, milk and water; the amount of the latter was not restricted.

The total nitrogen in the meat and milk was estimated by Kjeldahl's method. A considerable amount of meat was minced, and mixed into a uniform mass; a sample of this was analysed,

and the rest kept in an ice chest; the cats received a definite quantity each day.

The urine was analysed daily; the fæces were collected for several days, and the total nitrogen present estimated. The total nitrogen of the urine and fæces was estimated by Kjeldahl's method, the urea by a modification of Folin's method, the ammonia by Schaffer's method, and the creatinin by the colorimetric method of Folin. All the analyses were made in duplicate.

RESULTS.

The effects of removing portions of the kidneys may be grouped as follows:—First, the general conditions of the animals, including changes in body weight; secondly, the nitrogenous metabolism; thirdly, alterations in the amount and concentration of the urine.

1. *The condition of the animals.*—After the first operation, the cats usually drank a little milk on the same day, but for several days their appetite was poor, and they lost weight. Eventually they ate very well, and appeared to be more hungry than normal cats. For a day or two the urine contained blood, and for another two or three days albumen was present.

Three cats survived the second operation for some time; they rapidly recovered from the anæsthesia, and showed very little shock.

Two of the three cats ate very little after the second operation, and refused food altogether during the last few days of life; the third cat ate well for ten days, when its appetite also failed.

Vomiting and diarrhœa were observed in all the cats, and they seemed very susceptible to cold. They acquired a very foul breath, and soreness of the lips and gums; their fur came off very rapidly.

Cat 1 lived six days, cat 2 lived seven days, and cat 3 lived seventeen days after the second operation. The rectal temperature was maintained at 100° or more until the last few days of life.

The body weight.—It will be seen from the following table that normal cats lose weight when kept in confinement, notwithstanding some exercise daily. The loss of weight, however, is less than that observed in Rose Bradford's dogs, most of which lost 10 per cent. or more of their initial weight before the first operation. In our experiments, the cats were not put into the collecting cage before the first operation, so that this initial loss of weight was avoided.

TABLE I.

	Initial weight.	Final weight.	Loss.	Time in cage.
	grammes.	grammes.	per cent.	days.
Normal cat ...	3650	3580	1·9	19
Normal cat ...	2300	2140	6·9	8

The effect of the two operations upon the weight of the cats is shown in the following table:—

TABLE II.

	Initial weight, first operation.	Weight at time of second operation.	Loss.	Final weight.	Loss.	Life after second operation.
	grammes.	grammes.	per cent.	grammes.	per cent.	days.
Cat 1 ...	2420	2120	12·3	1600	33·8	6
Cat 2 ...	2880	2550	11·4	1840	36·1	7
Cat 3 ...	2500	2220	11·2	1640	34·4	17

The final percentage loss of weight is much the same, and was reached in cat 3 in seventeen days, and in a much shorter time in the other cats, because cat 3 ate well for ten days, whereas the others ate very little after the second operation. These figures correspond closely with those of Rose Bradford; he also found that the animals lived much longer after the second operation when they took food.

2. *The nitrogenous metabolism.*—The total nitrogenous metabolism was determined in three cats before and after the second

operation; the urinary nitrogen was also estimated in one of these cats before the first operation. The results are summarised in the following protocols:—

Cat 1.—October 12. Weight 2420 grammes. Removed part of left kidney, weight, 6·8 grammes.

Date.	Weight.	Total N. in urine.	N. as urea.	N. as ammonia.	N. as creatinin.	N. in food.
	grammes.	grammes.	per cent.	per cent.	per cent.	grammes.
Oct. 26	2130	1·69	—	3·9	1·6	3·0
" 27	2160	3·44	90	4·3	1·7	3·0
" 28	2090	1·09	—	2·2	1·5	2·6
" 29	Removed right kidney: weight 10·5 grammes.					
" 30	2050	0·94	74	2·6	2·3	} 0·83
" 31	1950	0·86	90	1·6	2·4	
Nov. 1	1820	0·84	—	3·6	2·7	
" 2	1770	1·73	—	2·0	2·0	
" 3	1660	1·02	70	6·0	1·6	
" 4	1600	Found dead.				

	N. intake.		N. output.		Fæces.
	Total.	Average.	Total.	Average.	
After first operation —3 days' period...	grammes. 8·5	grammes. 2·84	grammes. 6·22	grammes. 2·07	gramme. 0·59
After second operation —6 days	1·2	0·2	5·71	0·95	0·52

Post-mortem.—No evidence of sepsis. Some subcutaneous fat still present. Remainder of kidney weighed 3·8 grammes.

Total kidney weight.....=20·6 grammes.

Amount after second operation (3·8 grammes)=less than $\frac{1}{4}$ total kidney weight.
=1·5 grammes
per kilo.

Cat 2.—October 19. Weight, 2880 grammes. Removed part of left kidney, 8·8 grammes.

Date.	Weight.	Total N. in urine.	N. as urea.	N. as ammonia.	N. as creatinin.
	grammes.	grammes.	per cent.	per cent.	per cent.
Oct. 26	2600	2.65	73.9	3.8	1.4
Nov. 1	2510	3.08	92.8	3.3	1.7
" 8	2550	3.43	79.9	—	1.2
" 4	2550	3.59	—	3.8	1.4
" 5	Removed right kidney, weighing 14.1 grammes.				
" 6	2450	1.10	88.2	3.4	2.2
" 7	2380	1.69	84.0	1.6	2.1
" 11	2000	1.79	89.9	2.0	1.2
" 12	Cat moribund.	T. 95°-0.	Killed by chl	oroform.	Weight 1840 grs.

	N. intake.		N. in urine.		Total N. in faeces.
	Total.	Daily average.	Total.	Daily average.	
	grammes.	grammes.	grammes.	grammes.	grammes.
After first operation —Period of 10 days	89·7	3·9	29·01	2·9	2·26
After second operation—6 days.....	4·46	0·74	8·78	1·46	1·0 (approx.)

Post-mortem.—Remainder of kidney adherent to spleen, normal in appearance, very little omental fat; none visible elsewhere. Muscles not obviously wasted. No evidence of sepsis.

Total kidney weight..... = 29·6 grammes.

Weight found *post mortem* = 6·7 "
 = $\frac{2}{9}$ total kidney weight.
 = 2·3 grammes per kilo.

Cat 3.—September 4. Weight, 2500 grammes. Removed part of left kidney—4 grammes.

Date.	Weight.	Total N. in urine.	N. as urea.	N. as NH ₃ .	N. as creatinin.	N. intake.
	grammes.	grammes.	per cent.	per cent.	per cent.	grammes.
September 11...	2140	3.52	—	3.1	1.3	10.4
" 12...	2120	4.51	88.8	4.5	—	7.6
" 16...	2220	5.12	90.1	3.6	1.3	7.8
" 19...	Removed right kidney, wt. 10.25 gms.; wt. of cat, 2220 gms.					
" 23...	2020	3.26	75.0	9.9	2.0	9.0
October 2.....	1890	1.13	83.1	10.0	1.7	nil
" 5.....	1670	0.89	—	2.0	1.1	nil

After the second operation, the cat ate well for twelve days; after that it ate very little and wasted rapidly. It was moribund on October 6, and was killed by chloroform. Weight at death 1640 grammes.

Post-mortem.—There was no sepsis; very little fat was visible in the subcutaneous tissues.

Total kidney weight.....=20.65 grammes.

Amount left *post-mortem*=6.4
 = less than $\frac{1}{3}$ total kidney weight.
 =2.5 grammes per kilo.

	Total N. intake.	Daily average.	Total N. in urine.	Daily average.
	grammes.	grammes.	grammes.	grammes.
After first operation— 8 days' period.....	25.2	3.4	11.3	3.77
After second operation— First 6 days.....	23.4	3.9	12.86	2.14
Second 6 days.....	24.2	4.03	16.0	2.6
Last 4 days.....	0	0	3.72	0.93

The nitrogen intake for cat 3 is not absolutely exact, since the meat and milk were not analysed every day.

The clinical condition of these cats was apparently identical with that of Rose Bradford's dogs; in both cases, the second

operation was usually followed by rapid wasting. In two of the three cats considerably more than three-quarters of the total kidney weight was removed; in the third cat rather less than three-quarters was removed, but since the animal died, one may conclude that cats need rather more kidney than dogs in order to maintain life. In this connection it may be noted that in cats the average kidney weight is 9.1 grammes per kilo., as compared with 6.7 grammes per kilo. in dogs.

There is no doubt, then, that the experimental conditions of Bradford's dogs were strictly reproduced. Yet one of the cats showed no increased output of nitrogen after the second operation; in one cat the increase of nitrogen first occurred five days after the operation, when the cat had lost 28 per cent. of its weight, and was almost moribund; and in the other cat the increase occurred four days after the operation, when the loss of weight was 22.5 per cent.

In none of the cats did the nitrogen output after the second operation ever reach that observed after the first operation, and it never greatly exceeded that found in normal fasting cats. The greatest daily output of urinary nitrogen after the second operation, when the cats refused food, was 1.79 in cat 2 on the last day of life. For normal cats kept without food for twenty-four hours, the output of urinary nitrogen is about one gramme, and the loss of weight about 100 grammes.

The protocols, moreover, show that the second operation has no appreciable effect upon the percentage of urea, ammonia, and creatinin relatively to the total nitrogen. There is no increase in the output of creatinin (on a milk diet) such as might be expected if muscular metabolism were excessive.

We find, therefore, that the removal of three-quarters of the kidney weight of cats has no influence upon their nitrogenous metabolism until the last two or three days of life. This terminal increase of nitrogen only occurs when the cats have lost 22 per cent. or more of their body weight, and are obviously in a state of inanition. The two cats which showed this terminal increase of urinary nitrogen ate very little after the second operation, and wasted rapidly.

The effect of starvation upon the body weight and urinary nitrogen of normal animals has been investigated by Voit, Schöndorff, Kaufmann, and others. It is clear, from a comparison of their results with the condition of our cats, that the condition of starving animals is identical with that of cats which refuse food after the second operation on the kidneys.

There is in both cases a progressive loss of weight, a fall of temperature during the last few days of life, and usually a terminal rise in the output of nitrogen in the urine. E. Voit and others have shown that, in starvation, the nitrogen output may increase several days before death, and that the time of its onset is directly related to the amount of fat originally possessed by the animal. A very fat animal may never exhibit the increase of nitrogen, whereas, if the original store of fat is small, a very few days of starvation suffice to evoke an increased output of nitrogen. For example, a starving dog, observed by Schöndorff, showed an increased output of nitrogen when it had lost 20 per cent. of its weight; in our cats the nitrogen rose coincidentally with a loss of 22 per cent. or more of the body weight.

We consider, therefore, that the wasting, fall of temperature and final increase of urinary nitrogen occur simply because the cats refuse food after the second operation; they die from inanition, and the rise of urinary nitrogen, when it occurs, merely means that the animal's store of fat is much diminished, and that more energy must be supplied by proteid breakdown.

We consider, further, that the same explanation fully accounts for the results obtained by Rose Bradford, and that there is no evidence from his experiments that the kidneys directly influence nitrogenous metabolism.

It may be added that Dr. Pembrey has investigated the gaseous exchange of these cats; he finds that his results are such as would be given by animals in a state of inanition.

3. *The amount and concentration of the urine.*—The amount and specific gravity of the urine of cats varies widely according to their diet. On a meat diet the urine is concentrated; on a milk diet it is abundant and dilute. Making allowances for variations of diet, we find no evidence that the amount and

specific gravity of the urine are necessarily modified by either the first or second operation. Only one cat almost invariably passed abundant quantities of dilute urine after the first operation; the others often passed a concentrated urine. In this respect our results are at variance with those of Rose Bradford; and it may be pointed out that the effect, even in dogs, is not a constant one, since in half of Bradford's experiments the urine was no more abundant after the second than after the first operation.

It may be concluded, therefore, that the increase in quantity and decrease in concentration of dog's urine, after operations on the kidneys, is an incidental rather than an essential result.

TABLE III.

	Nature of food.	Urine.		
		Amount.	Sp. gr.	Total N.
		c.c.		grammes.
Normal cat-	{ Meat	112	1046	5.4
	{ Bread & Milk...	810	1007	1.6
After first operation—				
Cat 1	{ Meat	128	1040	5.1
	{ Bread & Milk...	435	1008	1.55
Cat 2	{ Meat	164	1038	3.44
	{ Milk	124	1020	2.1
Cat 3	{ Meat & Milk...	68	1042	2.65
Cat 4	{ Meat	110	1040	?
Cat 5	{ Meat	48	1054	—
	{ Milk	150	1015	—
After second operation—				
Cat 1	{ Milk	90	1020	1.49
	{ Meat	182	1018	3.02
Cat 2	{ Milk	78	1030	0.94
	{ Milk	81	1018	1.07
Cat 3	{ Meat & Milk ...	100	1019	1.10
	{ Meat & Milk ...	208	1018	2.44

CONCLUSIONS.

1. We confirm Bradford's observations that removal of three-quarters or more of the total kidney weight in cats is followed by loss of appetite, wasting, and death within a few days or weeks.

2. We find that in such cats an increased output of nitrogen is not of constant occurrence; and that it takes place only in cats

which have lost 22 per cent. or more of their initial body weight at the time of its onset.

3. We conclude, therefore, that the kidneys have no direct influence upon nitrogenous metabolism, and that the increased output of nitrogen is simply the result of inanition, and is of the same nature as that observed in starving animals.

4. We find that, after removal of a portion of one kidney, and also after subsequent removal of the opposite kidney, cats are still able to pass a concentrated urine, and that the amount of the urine is not necessarily increased beyond the normal.

The expenses of this research were partly defrayed by a grant from the Grants Committee of the Royal Society, to whom we desire to express our indebtedness.

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SECRETIN IN RELATION TO DIABETES MELLITUS.

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SECTION I.

THE TREATMENT OF DIABETES WITH SECRETIN.

THE relationship between the pancreas and diabetes has long been recognised, and it has been supposed that many cases of diabetes result from the deficiency or absence of an internal secretion normally produced by the pancreas. Starling suggested that secretin might furnish the stimulus not only to the external, but also to this internal secretion, and that it might prove to be of value in the treatment of diabetes. But Spriggs, who injected intravenously once a day 5 c.c. of a secretin solution freed from depressor substance, obtained a negative result in a patient who died of coma a week after the treatment had been begun.

Recently Moore, working with Edie and Abram, has published the results obtained by giving secretin by the mouth to three patients suffering from diabetes. Their first case—a man aged 25—at the beginning of the treatment was passing 40–65 grms.

of sugar daily on a diabetic diet with phenacetin. He then received 30 c.c. of secretin solution three times daily. After a latent period of three weeks the sugar fell suddenly to 32 grms., and for several weeks varied from 21-30 grms. daily. After four months' treatment with secretin the urine became free from sugar, and the patient gained in weight. The patient returned to work, and the secretin treatment was discontinued. Six months later he returned to the Hospital suffering from phthisis. His urine contained about 120 grms. of sugar daily; secretin was again administered, but without effect. The other two cases were children aged seven and nine respectively. In the first, the secretin treatment was begun simultaneously with the administration of a rigid diabetic diet; the quantity of sugar in the urine gradually fell, and the urine became sugar free at the end of forty-six days. The second child was put upon a diabetic diet together with small quantities of carbohydrate; twelve days later treatment with secretin was begun, and in twenty-four days the urine was sugar free. Moore suggests that the extract of duodenal mucous membrane supplied to the pancreas a chemical excitant, which was lacking in the diabetic patients; this caused the pancreas to resume its formation of internal secretion, and, as a result, the patients regained the power of metabolising carbohydrate, and retained this power for some time after the omission of the secretin, but not of the strict diet.

In all of these cases the treatment by secretin was combined with a diabetic diet more or less rigid. It is necessary, therefore, to consider whether results similar to those observed by Moore are seen in similar cases of diabetes treated by dieting alone. Clinically, diabetes may be divided into two grades of severity, mild and severe. In the first, the dextrose in the urine appears to come only from the carbohydrate of the food. When such a patient is placed on a rigid diabetic diet, his urine may be expected to become sugar free within a week, and not to give a reaction with ferric chloride; the patient rapidly improves, and may regain a very considerable power of utilising carbohydrate food. The other type of the disease is different clinically, in that dextrose is still passed out, although the patient is having the

most rigid diet which can be devised. In the most severe cases the patient, when on an ordinary diet, passes out much sugar and diacetic acid; when placed on a rigid diet the sugar in the urine decreases for a time, but the diacetic acid and acid intoxication rapidly increase, so that within a fortnight the patient may suffer from nausea, loss of appetite, and other symptoms of threatened coma, from which he may or may not spontaneously recover. However long the strict diet is maintained, the sugar in the urine never disappears, and very often it tends to rise after the initial fall. None of Moore's cases were of such severity as this. The mildest cases of this type give a very different response to treatment by diet. Such patients, when on an ordinary diet, may or may not pass out diacetic acid besides sugar; when placed on a rigid diet, diacetic acid is passed and the sugar after fluctuations decreases, so that the urine may become sugar free in a month or two. Considerable power of utilising carbohydrate may be gained, the diacetic acid reaction may disappear, and the patient may pass for a time into the mild type of diabetes. From the histories of Moore's cases, and from the analyses of the urines given by Edie and Whitley, it would appear that cases 2 and 3 were of this nature, and that of the two, case 2 was rather the more severe. It is a well-known fact that cases rather more severe than either of these may become sugar free after a long period of dieting, but that if they go back to ordinary diet for several months and then come under treatment again, it may be found that the type of disease has undergone a considerable change for the worse; this appears to have happened in Moore's first case. In fact there is no evidence to show that any of Moore's cases were of such severity that dieting alone would not have accounted for the observed disappearance of sugar from the urine. It is desirable, therefore, to test the effect of secretin on diabetics of a rather more severe type.

Methods.—The extracts used were obtained from the intestinal mucous membrane of pigs, sheep, and other animals. The upper two or three feet of the intestine were used, and the extracts were made by the method described by Bayliss and

Starling. In a majority of cases the activity of the extracts was tested by experiment on animals and, if need arose, the extracts were concentrated. In the first instance the extract was injected subcutaneously in 10–20 c.c. doses, but the patients objected to the injections, as they caused much pain locally and sometimes severe headache; consequently, after one or two injections, the secretin was given only by mouth. Each patient received 30 c.c. two or three times daily, one hour after food. The total urine for the twenty-four hours was collected and measured each day; the sugar was estimated by Pavy's method, and the ferric chloride test for diacetic acid was made use of.

DESCRIPTION OF CASES.

We have treated three cases of the severe type of diabetes with secretin. Case 1 was clinically the least severe; case 3 was suffering from diabetes in its most severe form, and case 2 was rather less severe than this.

CASE 1.—A boy, aged 15, was admitted into Guy's Hospital on January 31st, 1906, for thirst and wasting. These symptoms had been noticed only since the previous December.

On admission the patient was found to be extremely thin; his urine contained a large amount of sugar, but neither acetone nor diacetic acid. For two days he was placed on an ordinary diet, and on February 2nd, this was changed to a rigid diabetic diet with the daily addition of 35 grams of carbohydrate given at dinner time in the form of potatoes. On February 26th, the daily allowance of carbohydrate was reduced to 25 grams. On February 28th, the urine began to give a reaction with ferric chloride, which disappeared on March 4th, when the urine contained only a trace of sugar. On March 5th, the urine became sugar-free after thirty-two days of treatment by dieting. Between February 2nd and March 1st, the patient received 20 grams of sodium bicarbonate daily; this was stopped, as the urine became alkaline to litmus on March 1st.

On March 6th, the patient was put back upon the ordinary full hospital diet, and on March 8th, 10 c.c. of secretin solution were injected subcutaneously. Between March 9th and 19th the patient received 30 c.c. of secretin solution by the mouth, either once, twice or three times a day. During this period the urine contained increasing quantities of sugar, but gave no diacetic reaction.

On March 20th, the patient was put on the most rigid diabetic diet which could be devised; it contained no milk, and the substitutes for bread used were protene bread and biscuits, and Callard's brown caseoid bread. The diacetic reaction in the urine returned at once, and the sugar diminished, but had not disappeared at the end of nine days.

The characters of the urine, the amounts of sugar passed, and other details are given in the following table:—

1906. Date.	Daily Amount of Urine in c.c.	Total Sugar in grams.	Dose of Secretin in c.c.	Weight of Patient in kilos.	Other Characters of Urine.
Jan. 31	1931	106.5*	—	—	Acid, no acetone nor diacetic acid.
Feb. 1	2397	203.6*	—	—	
" 2	Diabetic diet with 35 grams carbohydrate and 20 grams sodium bicarbonate.				
" 4	1130	113.4*	—	—	Acid, no acetone nor diacetic acid.
" 5	1760	101.9*	—	—	" " "
" 6	1470	91.8*	—	—	" " "
" 10	1470	81.5*	—	—	" " "
" 12	1820	103.7*	—	—	" " "
" 22	1480	47.4*	—	—	" " "
" 26	Carbohydrate reduced to 25 grams.				
" 28	2470	99.8	—	—	Acid, faint diacetic reaction.
Mar. 1	2850	105.8	—	—	Alkaline
" 2	1550	53.1	—	—	Neutral, weak "
" 3	890	14.8	—	34.5	Acid,
" 4	1220	Trace	—	—	no diacetic reaction.
" 5	1220	Absent	—	34.9	"
March 6th, the patient was given ordinary diet.					
" 6	2400	89.1	—	—	Acid, no diacetic reaction.
" 7	2360	147.5	—	33.1	" " "
" 8	2410	180.7	10(subcut.)	—	" " "
" 9	2620	218.9	30(mouth)	33.8	" " "
" 10	2540	205.7	30	—	" " "
" 11	3180	242.2	60	34.1	" " "
" 12	2660	216.5	60	—	" " "
" 13	2950	247.4	90	34.6	" " "
" 14	3530	273.3	90	—	" " "
" 15	2970	266.5	90	34.9	" " "
" 16	3130	288.2	60	—	" " "
" 17	2470	233.5	60	35.0	" " "
" 18	3280	330.6	60	—	" " "
" 19	2500	233.2	90	35.2	" " "
March 20th, patient was put on a rigid diabetic diet.					
" 20	1330	58.5	—	—	Acid, trace diacetic acid.
" 21	1370	17.8	—	—	" " "
" 22	1250	36.3	—	—	" " "
" 23	1510	45.8	—	—	" " "
" 24	1440	32.4	—	—	" " "
" 25	1610	54.0	—	—	" " "
" 26	1440	54.0	—	—	" " "
" 27	1230	34.5	—	—	weak, diacetic reaction.
" 28	1930	68.9	—	—	" " "

Estimations marked * were made by the Ward Clerk before the case came into our hands.

After leaving the hospital the boy went back to an ordinary diet for several months. Recently he has been under the observation of one of us; his urine contains much sugar and diacetic acid, and can no longer be made sugar free by a restricted diet.

CASE 2.—A man, aged 49, was admitted into Guy's Hospital on March 3rd, 1906, for cough and shortness of breath. He had been in the hospital previously, and was known to have suffered from phthisis and diabetes since December, 1903.

On admission the patient was found to be thin; he was suffering from chronic fibroid phthisis, and throughout his stay in the hospital showed no pyrexia; his urine contained a moderate amount of sugar, gave no diacetic acid reaction, and did not contain albumen. He was placed at once upon a rigid diabetic diet, together with 35 grams of carbohydrate given daily at dinner time in the form of potatoes. The same diet was continued during and subsequent to the period of treatment with secretin.

On March 6th, the urine began to give a reaction with ferric chloride, which increased in intensity until, on March 12th and 13th, it was a strong reaction; from this date the intensity decreased, and on March 21st, the reaction was only weak. On March 7th, the patient felt sick and lost his appetite; these symptoms of incipient coma lasted for two days, and did not recur.

On March 6th, 10 c.c. of secretin solution were injected subcutaneously, and on March 8th and 9th, 20 c.c. These injections gave the patient not only a severe headache, lasting several hours, but the last produced such a severe fall in the blood pressure as to be dangerous.

The output of sugar in the urine showed no tendency to diminish in amount during or after the period of treatment with secretin; on the whole it rose slowly and steadily throughout the period of observation.

The progress of the case is shown in the following table:—

1906. Date.	Daily Amount of Urine in c.c.	Total Sugar in grams.	Dose of Secretin in c.c.	Weight of Patient in kilos.	Other Characters of Urine.
Mar. 3	950	31.2	—	—	No diacetic reaction.
" 4	1420	45.3	—	—	" "
" 5	1570	52.3	—	—	Trace " "
" 6	1700	54.9	10 (subcut.)	—	Moderate diacetic reaction
" 7	1830	63.2	—	—	" " "
" 8	1900	65.1	20 (subcut.)	54.7	" " "
" 9	2160	79.0	20 (subcut.)	—	" " "
" 10	1670	62.2	30 (mouth)	54.2	" " "
" 11	1430	63.8	60	—	" " "
" 12	1970	75.2	60	55.2	Strong " "
" 13	1770	70.8	90	—	" " "
" 14	1810	88.7	90	54.2	Moderate " "
" 15	1850	89.8	90	—	" " "
" 16	1730	85.7	60	54.3	" " "
" 17	1630	81.8	60	—	" " "
" 18	1490	86.2	60	54.3	Weak " "
" 19	1630	85.3	90	55.0	" " "
" 20	1420	76.8	90	—	" " "
" 21	1920	86.5	90	54.9	" " "
" 22	2110	97.7	90	—	" " "
" 23	1650	85.9	90	54.8	" " "
" 24	1560	83.7	90	—	" " "
" 25	1270	70.2	—	54.9	" " "
" 26	1340	78.3	—	—	" " "
" 27	1260	71.3	—	55.9	" " "

CASE 3.—A man, aged 45, was admitted into Guy's Hospital on March 1st, 1906, for thirst, polyuria and wasting. The patient had been losing weight for about a year and had noticed polyuria for six months. His daughter, aged 8, had died in the hospital of diabetic coma just previously to his own admission. Her case is referred to as case 1 in section II. of this paper.

On admission the patient was found to be very wasted; his breath smelt strongly of acetone; his urine contained diacetic acid, acetone and a moderate quantity of sugar. He was placed at once on a rigid diabetic diet, together with 35 grams of carbohydrate given as potatoes. The same diet was maintained until the end of the period of observation.

On March 2nd, the urine gave a moderate reaction with ferric chloride; this increased to a strong reaction on March 6th, and continued so until the end. On March 7th, the patient complained of nausea, could eat very little and felt too ill to get up. The next day he vomited, ate practically no food, and was stupid and rather drowsy. On March 9th, the patient ate four ounces of ordinary bread and some milk; by the next day the symptoms of incipient coma had begun to disappear and the patient went back to his proper diet. On March 8th, the patient was given 15 grams of sodium bicarbonate; the dose was increased to 30 grams on the next day, and this quantity was given daily until March 19th, when the urine became alkaline to litmus; after this the drug was discontinued.

On March 6th, 10 c.c. of secretin solution were injected subcutaneously, and on the 8th, 20 c.c. After that date 30 c.c. were given once, twice, or three times daily by the mouth until 24th. During the first ten days of the treatment by secretin the amount of sugar in the urine varied but little, although on the whole it tended to increase; but on March 19th, the output became suddenly greater and continued at this higher level during the rest of the secretin treatment and after it was stopped. The striking alterations in weight were undoubtedly due to retention of water, following the administration of sodium bicarbonate; after March 16th, the daily quantity of urine rose and the stored-up fluid was got rid of.

The following table shows the progress of the case:—

1906. Date.	Daily Amount of Urine in c.c.	Total Sugar in grams.	Dose of Secretin in c.c.	Weight of Patient in kilos.	Other Characters of Urine.	
Mar. 2	2160	79.0	—	—	Acid, moderate	diacetic
" 3	2010	75.4	—	46.7	"	reaction.
" 4	2150	81.0	—	—	"	"
" 5	2430	83.4	—	47.2	"	"
" 6	2820	67.8	10 (subcut.)	—	strong	"
" 7	3290	86.1	—	47.2	"	"
" 8	2470	71.0	20 (subcut.)	—	"	"
" 9	2240	91.0	30 (mouth)	46.5	"	"
" 10	2150	96.9	30	—	"	"
" 11	2250	94.5	60	48.5	"	"
" 12	2580	97.0	60	—	"	"
" 13	2470	95.4	90	51.0	"	"
" 14	2350	89.4	90	—	"	"
" 15	2620	102.3	90	51.4	"	"
" 16	3330	120.6	60	—	"	"
" 17	3590	111.7	60	49.8	"	"
" 18	3600	108.4	60	—	Neutral	"
" 19	4300	152.3	90	47.7	Alkaline	"
" 20	3680	134.3	90	—	Acid	"
" 21	4210	162.8	90	46.8	"	"
" 22	4580	183.2	90	—	"	"
" 23	4600	184.7	90	47.1	"	"
" 24	4130	163.3	90	—	"	"
" 25	3950	145.2	—	46.8	"	"
" 26	4380	158.8	—	—	"	"
" 27	4050	154.6	—	—	"	"

CONCLUSIONS.

It will be seen from the preceding account that in three cases of the severe type of diabetes, the administration of secretin by the mouth had no influence whatever upon the output of sugar in the urine. And yet it was possible in case 1, after a latent period of more than a month, to abolish the glycosuria by means of dieting. It seems probable that Moore's cases were of a kind similar to this one, and that the long latent period, which he attributed to secretin, belonged to the diet. There appears to us to be no sufficient evidence that secretin, when given by the mouth, can abolish or influence the glycosuria of severe diabetes.

In the light of Starling's experience, that in animals secretin is not absorbed when introduced even in large amount into the alimentary canal, it seemed desirable to try the effect of full doses of secretin given subcutaneously. The number of subcutaneous injections given by us is too small to enable us to form any opinion of their value in the treatment of diabetes.

SECTION II.

PROSECRETIN IN DIABETES.

The treatment of diabetes mellitus with secretin is based primarily upon the assumption that prosecretin is deficient in, or absent from, the intestinal mucous membrane of either all, or at least some, diabetic patients. It seemed desirable to ascertain whether this assumption was justified by the facts. We have, therefore, examined for prosecretin the intestines of six diabetic patients. As a control, we have compared the results so obtained with those given by the intestines taken from nine patients dying of other diseases.

METHODS.

The duodenum and upper part of the small intestine was obtained from diabetic and other patients as soon as possible after death; the mucous membrane was scraped off, and an acid extract made according to the method described by Bayliss and Starling. The activity of the extract was tested by intravenous

injection into cats or dogs anæsthetised with ether or A.C.E. mixture, and having a cannula in the pancreatic duct. In every experiment the effect of the extract from diabetic mucous membrane was compared with that obtained by injecting secretin made either from normal animals or from non-diabetic patients. Many of the diabetic extracts were tested twice in different animals. As a rule, the blood pressure was recorded in the experimental animals, and the depressor effect observed. Further details appear in the protocols.

RESULTS.

(a) *Non-diabetic patients.*—It was necessary, in the first place, to determine whether prosecretin disappeared shortly after death or whether its presence could always be demonstrated in the duodenal mucous membrane, even one or two days post-mortem. The duodenum was taken from the bodies of nine patients at varying intervals after death; it yielded secretin in every case. The results of these control experiments are indicated in the following table:—

Case.	Sex, Cause of Death.	Interval after Death at which material was obtained and extracted.	Secretion of Juice obtained by Injection.
1.	Boy. Fibroid phthisis	46 hours	Fair.
2.	Woman. Uræmic coma	30 "	Fair.
3.	Man. Granular kidneys	25 "	Moderate.
4.	Woman. Mitral disease and phthisis	24 "	Abundant.
5.	Boy. Tuberculous meningitis and general tuberculosis	11 "	Fair.
6.	Man. Cirrhosis of liver	7 "	Fair.
7.	Child. Mastoid abscess and throm- bosis of lateral sinus	7 "	Abundant.
8.	Man. Pneumonia	6 "	Abundant.
9.	Woman. Carcinoma of pylorus. Gastro-jejunostomy; peritonitis	4 "	Fair.

From this table it is obvious that, although it is possible that there is some post-mortem disappearance of prosecretin, the duodenal mucous membrane contains a fairly large quantity of it as long as two days after death.

The following protocol, which will serve as an example, shows the presence of a normal quantity of prosecretin twenty-four hours after death:—

Experiment 4.—Woman, aged 20, died from mitral disease and phthisis. Duodenum obtained twenty-four hours after death; extract made at once in the usual way.

Injected 2 c.c. of the extract
into cat anæsthetised
with ether.

Blood pressure fell from 130 to 85
mm. Hg. Secretion of juice
0·5 c.c. Subsequent injections
yielded a similar secretion of
juice.

(b) *Diabetic patients.*—We have had the opportunity of examining the duodenum of six diabetic patients for the presence of prosecretin; three died of diabetic coma, and three died of inter-current disease. In view of the great importance of the clinical history in determining the grade and severity of the diabetes, we have given an account of each of these cases, in addition to the following general summary of the results obtained.

Case.	Sex, Age, and Cause of Death.	Clinical Duration of Disease.	Interval between Death and Preparation of Secretin.	Flow of Juice produced by Extract.
1.	Girl, aged 8. Diabetic coma	1 month	14 hours	Nil.
2.	Man, aged 27. Diabetic coma	22 months	14 "	1 drop from a maximal dose.
3.	Man, aged 30. Diabetic coma	10 "	35 "	Nil.
4.	Man, aged 48. Diabetes and phthisis	18 "	40 "	Very scanty.
5.	Woman, aged 58. Diabetes, coma and pyelonephritis	5 "	48 "	Moderate.
6.	Man, aged 67. Diabetes. Septicæmia	4 years	46 "	Very scanty.

CASE 1.—Girl, aged 8, was admitted into Guy's Hospital on February 21st, 1906, for wasting and thirst. Her father was subsequently admitted into the hospital suffering from severe diabetes, and is referred to as case 1 in section I. of this paper. She had been noticed to be getting thinner for five weeks, and had complained of thirst for three weeks. On admission she was found to be extremely thin; she was rather drowsy and showed slight "air-hunger"; her urine contained a trace of albumen, acetone, but no diacetic acid, 2·5 per cent. sugar; she passed 6·5 litres of urine in the first twenty-four hours. On February 25th, she became definitely comatose, and died the next day. The post-mortem took place seventeen hours after death; all the organs were found to be healthy, excepting that some of the mesenteric glands were large and caseous. The pancreas was soft and weighed 18 grams: microscopically it was normal.

The duodenum was received and extracted fourteen hours after death. The extract was tested upon a cat anæsthetised with ether, and compared

with extracts from non-diabetic case 4 and normal cat's intestines. The results are recorded in the following protocol :—

	Injection.	Blood Pressure.	Flow of Juice.
4 c.c.	extract from diabetic case 1 ...	130 fell to 80	Nil.
2 c.c.	" " non-diabetic case 4...	130 " 85	0·5 c.c.
5 c.c.	" " diabetic case 1 ...	110 " 70	Nil.
5 c.c.	" " " ...	110 " 60	Nil.
2 c.c.	" " non-diabetic case 4...	110 " 70	0·5 c.c.
4 c.c.	" " diabetic case 1 ...	110 " 70	Nil.
5 c.c.	" " normal cat ...	110 " 65	0·5 c.c.

CASE 2.—A man, aged 27, was originally admitted into Guy's Hospital on September 16th, 1904, for weakness, thirst and polyuria of two months' duration. On admission he was found to be thin; his urine measured about six litres, and contained 5 per cent. sugar, acetone and diacetic acid. He was dieted, and his urine became sugar-free on November 30th, and at the same time the diacetic reaction disappeared. The man left the hospital on February 16th, 1905.

He was readmitted on May 18th, 1906, for congenital lamellar cataract. He was passing daily about 20–30 litres of urine containing about 1·5 per cent. dextrose. On June 9th, he developed "air-hunger," and died, comatose, on the next day. The post-mortem examination showed that the body was much wasted, and that all the viscera were normal excepting for some old pleural adhesions; the pancreas weighed 54 grams, and was microscopically normal.

The intestines were received twenty-four hours after death, and an acid extract was made at once. The extract was tested upon a cat anaesthetised with ether, and compared with extracts made from the intestines of a normal dog and of a cat fourteen days after removal of the pancreas. The following protocol gives the results of the experiment :—

	Injection.	Blood Pressure.	Flow of Juice.
2 c.c.	extract from depancreatized cat...	150 fell to 70	0·5 c.c.
3 c.c.	" " patient ...	140 " 60	1 drop.
2·5 c.c.	" " depancreatized cat...	110 " 75	0·3 c.c.
2·5 c.c.	" " normal dog ...	145 " 60	0·7 c.c.
5 c.c.	" " depancreatized cat...	120 " 50	1·0 c.c.

The extract from this patient was tested thoroughly on two other animals, and gave generally no flow of juice at all, or in a few instances one drop, even when injected in doses of 10 c.c.

CASE 3.—Man, aged 30 years, was admitted into St. Bartholomew's Hospital for wasting and polyuria. He had been well until ten months previously, since when he had lost two stone in weight, and had passed large quantities of urine. While in the hospital he passed daily 3–5 litres of urine containing 100–200 grams of sugar; the urine contained diacetic acid. Eight days after admission the patient became comatose, and died twenty-four hours later. *Post-mortem*.—All the viscera appeared to be healthy, and showed very little post-mortem change. The pancreas weighed 65 grams; it was small and soft, and microscopically normal, excepting perhaps that the section showed slight excess of fibrous tissue round the small ducts in the gland.

The duodenum was obtained twenty-five hours after death, and an acid extract of the mucous membrane was made at once. A cat was anæsthetised with ether, and cannulæ were placed in the pancreatic duct and one jugular vein. The effects of injecting the extract from the patient's duodenum were compared with those yielded by normal dog's secretin, and are recorded in the following protocol:—

Time.	Injection.	Flow of Juice.
2-55 p.m.	Injected 3 c.c. extract from patient ...	Nil
2-58 "	" 3 c.c. normal dog's secretin ...	3 c.c.
3-31 "	" 3 c.c. extract from patient ...	Nil
4-3 "	" 3 c.c. " " " " ...	Nil
4-28 "	" 4 c.c. " " " " ...	Nil
4-35 "	" 3 c.c. normal dog's secretin ...	0·8 c.c.

The extract from the patient was concentrated and contained much depressor substance.

CASE 4.—Man, aged 48, was admitted into St. George's Hospital, under Dr. Ogle, on April 28rd, 1906, for phthisis and diabetes. His illness had begun gradually eighteen months previously with cough, loss of appetite, progressive wasting and thirst; he did not notice polyuria. On admission he was found to be extremely ill; the sputum contained tubercle bacilli; his legs were œdematous up to the thighs. His urine contained albumen, 8 per cent. dextrose, but not acetone. He was placed on a milk diet. The patient gradually became weaker and repeatedly vomited black blood. On April 28th he died from cardiac failure, not from diabetic coma.

The post-mortem examination was made twelve hours after death. Both lungs showed extensive active tuberculosis. The heart was enlarged on its right side. The liver weighed 53 ounces; it was fatty and nutmegged. The pancreas weighed 113 grains; it was normal microscopically. The stomach and intestines contained altered blood; no source of hæmorrhage could be found.

The intestines were obtained sixteen hours after death and were kept in ice for another twenty-four hours. An acid extract was then made in the usual way and tested on a cat anæsthetised with ether. The results were compared with that yielded by normal dog's secretin, as is shown in the following protocol:—

Nature of Injection.	Blood Pressure.	Flow of Juice
7 c.c. extract from patient ...	Fell from 155 to 75 mm. Hg.	Nil
6 c.c. normal dog's secretin ...	" " 150 " 80 " "	1 c.c.
8 c.c. extract from patient ...	" " 135 " 70 " "	2 drops.
10 c.c. " " " " ...	" " 130 " 70 " "	2 drops.

CASE 5.—Woman, aged 58, was admitted into St. Thomas's Hospital on May 4th, 1906, under the care of Dr. Acland, for diabetes. She had suffered from polyuria and thirst for five months, and had noticed loss of weight for three months. On admission, the patient was found to be well nourished. Her urine contained a trace of albumen, 3 per cent. sugar, and had sp. gr. 1036. She was placed upon a diet in which the carbohydrates were slightly restricted. On May 9th the patient became rather drowsy; the urine contained traces of diacetic acid and acetone. On the next day she was

more drowsy, and the urine contained more diacetic acid and acetone. On May 11th she died in a comatose condition. Her temperature was sub-normal throughout. At the post-mortem examination all the viscera were found to be healthy, excepting the kidneys, which contained a few small abscesses due to pyelonephritis. The pancreas was normal microscopically.

There is a doubt whether the coma in this case was diabetic or uræmic. The opinion of those who observed the case clinically was that the coma was not diabetic.

The intestines were obtained forty-eight hours after death, having been kept in ice most of the time. The duodenal extract was made in the usual way, and tested upon a dog, anæsthetised with A.C.E. mixture. As a control secretin from a normal dog and from a fatal case of pneumonia (case 8 of the non-diabetic patients) was injected. In the same dog the duodenal extract of diabetic case 6 was tested, and in the following protocol the results of both cases are given :—

Injection.		Blood Pressure.		Flow of Juice.
9 c.c. extract from non-diabetic case 8...	90	fell to 40 mm. Hg.		2.0 c.c.
8 c.c. " " diabetic case 5 ...	110	" 45 "		0.6 c.c.
8 c.c. " " normal dog ...	120	" 40 "		1.4 c.c.
9 c.c. " " diabetic case 6 ...	90	" 40 "		1 drop.
8 c.c. " " " "	90	" 40 "		1 drop.
10 c.c. " " " "	110	" 40 "		1 drop.
10 c.c. " " " "	90	" 40 "		1 drop.

CASE 6.—A man, aged 67, was admitted into Guy's Hospital on May 11th, 1906, in an unconscious condition. Four years previously he had begun to suffer from great thirst and an abnormally large appetite; one year later he developed cataract in each eye. He had not been feeling well for a week before admission, and on the day of admission he fell down unconscious. When admitted into the hospital he was found to be well nourished; his urine contained 1.5 per cent. sugar, diacetic acid and acetone, and amounted to six litres in the day; his condition was considered not to be due to diabetic coma. On May 12th he became conscious, but still remained very ill. On May 14th he showed marked orthopnoea, and his dyspnoea was clearly due to cardiac and general circulatory failure. On May 16th his temperature rose to 106° F., and on the next day his left knee-joint became inflamed; he passed about 150–200 grams of sugar daily. On March 18th both knee-joints were acutely inflamed, and a pericardial rub was noticed; the patient became semi-conscious and died on the next day.

The post-mortem examination showed that the man had died of septicæmia and acute septic pericarditis. The heart muscle was fatty, the arteries atheromatous, the liver fatty, and the kidneys tough. The pancreas weighed 80 grams; microscopically it was normal.

The duodenum was received forty-six hours after death, and an extract of it was made at once. The effect produced by the injection of the extract into a dog is shown in the protocol at the end of case 5.

CONCLUSIONS.

Our observations show that only in one out of six cases of severe diabetes was prosecretin present in an amount approximating to the normal. This one case, however, is sufficient to show that an absence of prosecretin is not a necessary result of the abnormal metabolism of severe diabetes. The same thing is shown by the fact that we found prosecretin present in normal quantity in the duodenum of a cat a fortnight after the removal of the pancreas (*vide* protocol at the end of case 2). The cat presented all the symptoms of diabetes in a severe degree; it had lost more than one-third of its original body weight, the urine gave a reaction with ferric chloride, and the $\frac{D}{N}$ was about 3.

In the other five cases of severe diabetes, prosecretin was either absent, or present in very small quantities; in the three cases of diabetic coma it was absent, and in two cases of severe diabetes, which died of intercurrent disease, it was present, but extremely scanty. There are two obvious hypotheses which could be advanced to account for the diminution or absence of prosecretin in these cases. In the first place, the acid intoxication, which almost invariably precedes the natural termination in coma, may prevent the normal production of prosecretin; on this view its absence would be a terminal result of the diabetes, and would be of very little importance clinically. Secondly, it is possible that prosecretin may be very deficient or absent from the outset in the more acute and severe cases of diabetes, which rapidly progress towards a fatal issue in coma; if this were true, the absence of prosecretin might be the actual cause of such cases of diabetes. But it would be necessary to assume also that secretin is the stimulus to the internal secretion of the pancreas, and that the pancreas is functionally, as well as microscopically, normal.

We have attempted to decide between these two hypotheses by producing an artificial acid-intoxication in animals, and then examining their intestines for the presence of secretin. For this purpose rabbits were used, and dilute phosphoric acid was administered by the alimentary canal; the alkalinity of blood-

serum was estimated by Wright's method, and is expressed as the strength of sulphuric acid necessary to neutralise it.

Experiment.—Rabbit.

Date 1909.	Weight in grams.	Alkalinity of Blood-Serum.	Quantity of Phosphoric Acid.
July 9	4200	$\frac{N}{20}$ (before treatment)	100 c.c. 1%, given per rectum.
" 10	3970	—	200 c.c. 1%, given per rectum in two doses, one in morning and one in evening.
" 11	3900	—	100 c.c. 0.5%, by mouth and 100 c.c. 1 % per rectum. (Animal seemed ill and very feeble).
" 12	3840	$\frac{N}{50}$	

Rabbit killed. Post-mortem, the stomach and duodenum were normal in appearance. Secretin was prepared from the duodenum in the usual way and its activity tested on a cat, anæsthetised with ether; secretin made from a normal rabbit was used as a control.

Injection.						Flow of Juice.
5 c.c. extract from normal rabbit	0.7 c.c.
5 c.c. " " injected "	0.6 c.c.
5 c.c. " " normal "	0.5 c.c.
5 c.c. " " injected "	0.4 c.c.

This experiment shows that prosecretin is not abolished by an acid intoxication which differed not in degree but only in duration from that observed in cases of severe diabetes. In human diabetes the duration of the acid-intoxication may extend over months; and it is possible that such a prolonged acidosis may destroy or inhibit the formation of prosecretin. On the other hand, it is equally possible that a deficiency of prosecretin may be casually related to diabetes. If this were so, it would follow that diabetes should result from an experimental reduction of the prosecretin in the intestines; and we are attempting to investigate this point. Until more evidence is forthcoming it is impossible to reach a conclusion as to the nature of the relationship existing between prosecretin and some cases of diabetes.

We wish to express our indebtedness to the Physicians of Guy's Hospital, to Dr. Acland, Dr. Ogle, and to Dr. Andrewes

of St. Bartholomew's Hospital, for their kindness in supplying us with clinical cases and post-mortem material.

Part of the expense of this investigation was defrayed by a grant from the Royal Society. The results have been published in the *Bio-Chemical Journal*, vol. i., as well as here.

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THE DIASTATIC FERMENT IN THE TISSUES IN DIABETES MELLITUS.

By F. A. BAINBRIDGE, M.A., M.D.,

AND

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A STRIKING fact observed in experimental diabetes after removal of the pancreas is the great diminution in the hepatic glycogen, notwithstanding the hyperglycæmia. Observations on the amount of glycogen present in the livers of diabetic patients are difficult to obtain and few in number; but the quantity present appears to be less than normal. On Bernard's hypothesis, the conversion of glycogen into dextrose is carried out by a diastatic ferment normally present in the liver. It is possible that the conversion of dextrose into glycogen also is effected by an enzyme, which might be either the diastatic ferment acting in a reverse way, or a different ferment altogether. The apparent inability of the liver in diabetes to store glycogen might be due to the absence of the necessary ferment. We have investigated the livers, blood and muscles of diabetic patients and of depancreatized cats, in order to ascertain whether they possess the normal diastatic ferments; and this we have found to be the

case. The further question, whether it can be shown that the normal liver possesses a ferment which can act synthetically upon dextrose, and if so, whether this ferment is present or absent in diabetes, is under investigation.

METHODS.

Preparation of the tissue extracts. Pavy has shown that pieces of liver, kept under alcohol for months, still contain an enzyme capable of converting glycogen into sugar. Our method of obtaining the ferment is based upon this observation, and is a modification of that employed by Pick. Miss Tebb has shown that the enzyme acts not only upon glycogen, but also upon starch; and in most of our experiments we have used Kahlbaum's pure soluble starch, as being more convenient to work with. In a few experiments we have used solutions of Merck's pure glycogen and obtained the same results as when using soluble starch.

Portions of liver, obtained as soon as possible after death, were minced and placed under five times their volume of 95 per cent. alcohol for several weeks. In the animal experiments, the liver was washed out and freed from blood before being minced and placed under alcohol. The alcohol finally was filtered off, and the liver washed with alcohol until the washings were free from sugar. The liver then was dried at 37° C., powdered and rubbed up with sand and water; some toluol was added, and the extraction was continued at 37° C. for twenty-four hours, during which time the flask was frequently shaken. The extract was filtered and yielded a clear yellow filtrate, which gave no colour reaction with iodine, and which contained small quantities of protein and sugar. Known quantities of this filtrate were incubated with a solution of soluble starch for twenty-four hours; an abundance of toluol was added. The solutions were then boiled in order to coagulate the protein and drive off the toluol; they were cooled, made up to a known volume and filtered. The filtrate was tested with iodine, and the amount of copper reducing substance present in it was estimated by Pavy's method, and the result is expressed as dextrose.

The blood used for extraction was received, during life, direct into alcohol. The subsequent procedure was identical with that described above in the case of the liver.

The muscle extract was made in the following way :—

In the animal experiments the muscles were washed, directly after death, as free from blood as possible by means of normal salt solution injected through the aorta. In the case of diabetic patients the muscles were not freed from blood. Portions of muscle were minced and pounded, first with sand and a little water, and then with Kieselguhr, until a nearly dry powder was obtained. This was exposed to pressure in a Buchner's press, and the muscle juice collected. The juice was then examined for the presence of ferment.

The extract of pancreas added to the other extracts in certain experiments corresponded to that described by Cohnheim, and was essentially a boiled watery extract of pig's pancreas, which had previously been minced and pounded up with sand. The strength of the extract was such that 2 c.c. of the solution contained the extract of about 1 grm. of pancreas.

EXPERIMENTS.

The presence in the liver, under normal conditions, of an enzyme capable of converting starch or glycogen into dextrose is so well established that we merely examined a few livers taken from normal animals and from the post-mortem room in order to demonstrate, firstly the effectiveness of the method of extraction, and secondly the existence of the enzyme in the livers twenty-four hours or more after death.

Two of the post-mortem cases are recorded here :—

CASE 1.—Liver, obtained twenty-four hours after death, from a patient who died two hours after an accident which fractured his vertebral column. 25 c.c. of the liver extract were added to 30 c.c. of 1 per cent. solution of soluble starch, toluol was added, and the whole was incubated at 37° C. for twenty-four hours. The control flask was boiled for several minutes before the toluol was added. At the end of twenty-four hours the flasks were boiled, cooled, made up to 100 c.c., and filtered. The following table gives the result obtained :—

	Iodine Test.				Sugar by Pavy.
Control	Blue	0·06 grm.
Unboiled flask	Violet	0·18 grm.

CASE 2.—Patient died of a cerebral tumour; liver obtained forty-eight hours after death. Experiment carried out in the same way as above.

			Iodine Test.		Sugar by Pavy.
Control	Blue	...	0·075 grm.
Unboiled flask	(1)	...	Violet	...	0·18 grm.
"	(2)	...	Violet	...	0·20 grm.

As regards the blood of normal men and animals, it has been shown by Ascoli and Bonfanti that a diastatic ferment is often present; and we have confirmed this in the case of the dog by the above method.

The muscle juice of normal animals possesses a feeble diastatic power. An experiment is recorded later which shows this effect in the dog.

(a) *The liver extract in diabetes.*—We have examined the livers of four diabetic patients and of four depancreatized cats. The full clinical histories of the patients have been given in the preceding paper; the cases are not numbered consecutively, but have received the same numbers in this paper as they had in the previous one. The cats had undergone almost complete removal of the pancreas, and showed in each case well-marked symptoms of diabetes; their urine contained an abundance of sugar and gave a feeble reaction with ferric chloride.

The method employed was the same in all cases. Thirty c.c. of liver extract were added to 40 c.c. of 1 per cent. solution of soluble starch; toluol was added, and the mixture incubated for twenty-four hours at 37° C. In some experiments a second flask contained the same mixture, with the addition of 10 c.c. of pancreatic extract, which corresponded to about 5 grms. of pancreas. The control flask was boiled before the addition of toluol. In some cases a fourth flask, containing liver extract with water and toluol, was incubated. The following table gives the results obtained:—

Case.		Liver extract and water.	Boiled control.	Liver extract and starch at 37°.	Liver extract, starch, and pancreatic extract at 37°.
2. Diabetic Coma.					
	Iodine No colour	Blue	No colour	—
	Sugar by Pavy 0.05 grm.	0.05 grm.	0.24 grm.	—
3. Diabetic Coma.					
	Iodine No colour	Blue	Violet	—
	Sugar by Pavy 0.06 grm.	0.06 grm.	0.26 grm.	—
5. Diabetes and Phthisis.					
	Iodine —	Blue	Violet	Violet
	Sugar by Pavy —	0.09 grm.	0.21 grm.	0.20 grm.
6. Diabetes and Septicæmia.					
	Iodine No colour	Blue	Violet	—
	Sugar by Pavy Trace	Trace	0.18 grm.	—
Cat A.					
	Iodine —	Blue	Violet	Violet.
	Sugar by Pavy —	Trace	0.10 grm.	0.12 grm.
Cat B.					
	Iodine —	Blue	Violet	Violet.
	Sugar by Pavy —	0	0.18 grm.	0.18 grm.
Cat E.					
	Iodine No colour	Blue	Violet	—
	Sugar by Pavy 0	0	0.12 grm.	—
Cat F.					
	Iodine No colour	Blue	Violet	Violet.
	Sugar by Pavy 0	0	0.11 grm.	0.12 grm.

The presence of sugar in some of the boiled controls indicates that the corresponding livers contained both glycogen and a ferment capable of converting glycogen into sugar.

(b) *The muscle juice in diabetes.*—Muscle was obtained from two patients, cases 2 and 3 in the previous table, and from cat E. The same method was used throughout. Eight c.c. of muscle juice were added to 20 c.c. of 1 per cent. solution of soluble starch; toluol was added, and the mixture incubated for thirty hours at 37° C. A second flask contained the same solutions, together with 10 c.c. of pancreatic extract. The control flask was boiled for several minutes before the toluol was added. At the end of thirty hours the flasks were boiled, cooled, made up to 100 c.c., and filtered. The following table of results contains, also, those obtained with the muscle of a normal dog.

Case.	Boiled control.	Muscle juice and starch at 37°.	Muscle juice, starch and pancreatic extract at 37°.
2. Diabetic Coma.			
Iodine	Blue	Violet	Violet.
Sugar by Pavy ...	0	0·11 grm.	0·12 grm.
3. Diabetic Coma.			
Iodine	Blue	Violet	Violet.
Sugar by Pavy ...	0	0·05 grm.	0·05 grm.
Cat E.			
Iodine	Blue	Blue	Violet.
Sugar by Pavy ...	0	0·03 grm.	0·05 grm.
Normal Dog.			
Iodine	Blue	Violet	—
Sugar by Pavy ...	0	0·04 grm.	—

(c) *The blood extract in diabetes.*—Blood was obtained during life from three diabetic patients, and from one depancreatized cat. One of the patients was case 2 in the previous tables, and his blood was obtained when he was in coma. The two other patients were suffering from severe diabetes. When their blood was taken they were being treated by secretin given by the mouth. Their full clinical histories have been given in the preceding paper, where they are referred to as cases 2 and 3. It may be mentioned that case 3 died of diabetes in November, 1906, eight months after our observations upon him were made.

The blood was treated and its diastatic activity observed by the method already described, so that it is unnecessary to give more than a table showing the results obtained.

Case.	Boiled control.	Blood extract and starch at 37°.
(1) Diabetic coma.—Case 2.		
Iodine	Blue	No colour.
Sugar by Pavy ...	Trace	0·11 grm.
(2) Severe diabetes.—Case 2.		
Iodine	Blue	Blue and Violet.
Sugar by Pavy ...	Trace	Too little to estimate.
(3) Severe diabetes.—Case 3.		
Iodine	Blue	Blue and Violet.
Sugar by Pavy ...	Trace	Too little to estimate.
(4) Cat E.		
Iodine	Blue	Violet
Sugar by Pavy ...	0	0·15 grm.

The almost complete absence of a diastatic ferment seen in the two cases of severe diabetes has also been observed by Ascoli and Bonfanti in some healthy human beings and animals.

CONCLUSIONS.

The livers and muscles of diabetic patients and of depancreatized cats contain a diastatic ferment. No attempt was made to ascertain whether the amount of enzyme present was greater or less than that found in normal animals. In two cases a diastatic ferment was found in the blood, and in two others it was absent. No evidence was obtained that the activity of the diastatic ferment of liver or muscle is increased by the addition of a boiled extract of pancreas.

Part of the expense of this investigation was defrayed by a grant from the Royal Society; and the results have also been published in the *Bio-Chemical Journal*, vol. ii.

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GASTRO-JEJUNOSTOMY.

By R. P. ROWLANDS, M.S.

ALTHOUGH this operation is a very valuable one in suitable cases, it is necessary to protest against its indiscriminate use or abuse. There are some who seem to think that gastro-jejunostomy cures all the ills that the stomach is heir to; and from the writings of others we may fairly ask with Porter,¹ why we are not all born with a gastro-jejunostomy?

Let us not forget that the stomach and duodenum have their uses in digestion and absorption, and that we ought not to endeavour to empty the one prematurely, or to occlude the other without due consideration, unless there is definite pyloric or duodenal obstruction, for which short-circuiting is of undoubted value. It has been frequently stated of late that gastro-jejunostomy is almost devoid of danger, but this is far from true, although it may be almost safe in the hands of experts if the patients are in fair general health, but the operation often has to be performed under very different circumstances from these. It is certain that many gastro-jejunostomies are now performed unnecessarily, and it is just as certain that many others are deferred until it is too late to secure the best results. The statistics of the former give a false idea of safety, and those of the latter are too unfavourable. The truth lies between them, and it can be fairly estimated that the average mortality of

¹ Annals of Surgery, 1907, vol. 44, p. 901. Dr. Porter gives many reasons for believing that gastro-jejunostomy is not a harmless operation, and his article is well worthy of careful consideration.

gastro-jejunostomy for non-malignant disease, as now performed by surgeons of average skill upon hospital and private patients, is nearer 6 than 2 per cent.; but when the operation is undertaken for simple gastric ulcer, and not for recurrent severe hæmorrhage, or for late pyloric stenosis, or other sequelæ, the mortality should certainly be well under 3 per cent. in the hands of aseptic surgeons of average skill and thorough practical knowledge of the details of technique which are essential to success.

In the practice of a few surgeons of unusual experience of gastric surgery the mortality may be even under 1 per cent. It must not be forgotten, however, that these surgeons have gradually acquired special skill and judgment, and especially that their fame enables them to get their cases earlier² than the average surgeon, who is often not asked to operate until it is too late to hope for the excellent immediate and remote results that can be obtained by operating in time to prevent the late results and grave complications of gastric ulceration. The general health of these neglected patients has been undermined by years of malnutrition, and the local conditions are often too seriously advanced for complete recovery to be expected. It is partly for these reasons that some hospital statistics, extending back for about ten years, and showing a mortality rate of over 20 per cent., should not be allowed to influence us too much when we are considering the death-rate of gastro-jejunostomy, as it is, or should be, performed at the present day. Moreover, these figures include the early failures from errors and imperfection of technique. Most of the operations were performed for sequelæ that should become more and more uncommon in the future.

In private practice the results are much better, for the patients generally seek relief earlier, and are in a better condition to undergo the operation.

The late results of gastro-jejunostomy are not so very good as some would have us believe, although they should certainly improve in the near future. It may be expected that the after-

² This can be very clearly seen by studying the statistics which were brought before the Royal Medico-Chirurgical Society in November, 1906.

results will be very good in about 70 per cent. and fair in about 20 per cent. of the non-malignant cases.

When performed for *malignant disease*, the mortality may be estimated to be about 15 per cent. in the hands of good surgeons. I am aware that some hospital statistics have shown death-rates of 40 per cent., but these results are largely due to the reasons already given. Moreover, the operation has frequently been performed in hopeless cases, with the object of relieving pain. It is clear that if the last days of these patients can be made less terrible, the operation should be performed regardless of statistics. On the other hand, experience has shown that the operation has been performed far too frequently, and it has, by this time, enabled us to make a wiser selection of cases. The ultimate results of gastro-jejunostomy for malignant disease are poor, although in selected cases the operation gives great immediate relief and may prolong life for some months.

The operation is to be avoided in all cases of gastric neurosis. To perform it for the crises of locomotor ataxy, or for the vomiting of early phthisis, can only be due to gross carelessness in diagnosis. That these and similar mistakes should have been made only emphasises the fact that this valuable operation is in considerable danger of being too frequently and too lightly undertaken, and that a very thorough examination should precede it in every case.

INDICATIONS FOR THE OPERATION.³

1. *Malignant disease of the stomach or duodenum.*—The operation is worse than useless when the growth does not cause obstruction of the pylorus and stasis of the gastric contents. It is to be hoped that with earlier exploration and diagnosis gastro-jejunostomy will be replaced to a greater extent by resection, although many patients will always present themselves so late

³For a much fuller discussion of the indications for gastro-jejunostomy, *vide* "The Operations of Surgery," Jacobson & Rowlands, 1907, vol. ii., pp. 460 and 494.

that only a palliative operation can be performed. At present many come too late even for this.

2. *Non-malignant diseases of the stomach and duodenum.*

i. *Pyloric stenosis.*—In most cases of pyloric stenosis, especially when there is great dilatation of the stomach, much thickening of the pylorus, extensive adhesions or active ulceration. Under these circumstances, and especially when the stomach is greatly dilated, posterior gastro-jejunostomy with a large opening is the best operation, and provides far better drainage than any pyloric operation, even those of Finney and Kocher.

ii. *In chronic ulcer of the stomach or duodenum causing severe and recurrent hæmorrhage, in spite of careful medical treatment.*—For the large majority of surgeons and patients, if not for all, it is not wise to perform gastro-jejunostomy or any other operation during the progress of severe gastric or duodenal hæmorrhage. The operation should be deferred until the attack of bleeding is over. Mr. Paterson estimates that the mortality of operations performed during hæmorrhage is about 80 per cent., whereas only about 5 per cent. die from one severe hæmorrhage, when only medical treatment is adopted during the attack. Gastro-jejunostomy performed in the *interval* does usually, but not always, prevent the recurrence of hæmorrhage. If an ulcer is discovered, inversion of it by sero-muscular sutures, as advised by Mr. Moynihan, should supplement the gastro-jejunostomy.

iii. *For chronic or relapsing ulceration of the stomach or of the duodenum after medical treatment has been thoroughly tried and has failed.*—The operation is especially to be recommended for the relief of the severe pain of duodenal ulcer, which generally ceases when the food has a large alternative exit from the stomach, and no longer need pass, to any considerable extent, over the ulcer. For chronic ulcer of the stomach the operation may succeed or may fail. When the opening is a very large one it generally succeeds, for it prevents distension of the stomach and the accumulation of the very acid gastric juice within the stomach, which

are the two main factors preventing the healing of the ulcer. When a chronic ulcer of the stomach is accessible, and can be removed without adding considerably to the risk of the operation, it is probably wise to excise it, in addition to performing gastro-jejunostomy.

Space does not allow a full consideration⁴ of this important question, but it may be stated that if definite symptoms of gastric ulcer, or especially of duodenal ulcer, do not disappear under a six months' course of thorough medical treatment,⁵ or if they soon reappear after the cessation of this treatment, posterior gastro-jejunostomy is strongly indicated in order to prevent the development of a chronic ulcer, with its dangerous and crippling complications and sequelæ, the most important of which are perforation, with peritonitis or subdiaphragmatic abscess, hæmorrhage, pyloric stenosis, hour-glass stomach, and perigastric adhesions.

It is sometimes wise to operate earlier in poor patients, because of the great difficulties in the way of continuing medical treatment long enough to effect a cure. The older the patient the more important is it to operate without avoidable delay. It should be added, however, that the operation should be performed by a good surgeon, otherwise the danger may be greater than by leaving well alone.

iv. *Infantile hypertrophic stenosis of the pylorus.*

v. *Hour-glass stomach.*

vi. *Tetany of gastric origin.*

The writer has discussed the question of operations for these conditions elsewhere.⁶

vii. *Perforated gastric ulcer.*— Finding it impossible to close a perforation, Braun successfully performed anterior gastro-jejunostomy, with the view of lessening or preventing leakage through the perforation. Mr. Paterson (Hunterian Lectures, *Lancet*, vol. i., 1906) considers that drainage by

⁴ For a fuller discussion, loc. supra cit.

⁵ Vide Hawkins, Spriggs, and others, *Medico-Chirurgical Transactions*, November and December, 1906.

⁶ Loc. cit., p. 499.

means of gastro-jejunostomy deserves a thorough and extended trial as a routine treatment of perforated gastric ulcer. He maintains that this may prevent subsequent troubles from persistence of ulceration, hæmorrhage, or secondary perforation of the same or of another ulcer. He also states that a more thorough closure of pyloric ulcers will be possible without risk of stenosis, that the rest given to the stomach promotes healing of the perforation, and that earlier feeding and administration of purgatives can be allowed. He also quotes Finney, that in 20 per cent. the perforations are multiple, and that gastro-jejunostomy may save these cases even if a perforation be missed. The most important and to my mind sufficient objection is that these patients are rarely in a condition to stand a prolongation of the operation when they come for treatment. If a gastro-jejunostomy becomes necessary it is safer in the great majority of cases to do it at a second operation. In some very early, and especially in pyloric or duodenal perforations, a gastro-jejunostomy may be primarily performed. Dr. Herbert French (*Med.-Chir. Trans.*, November, 1906) was able to trace and examine eighteen out of thirty Guy's Hospital patients who had recovered after operations for perforated gastric ulcers. Fifteen of these patients were wonderfully well in every way, but the three others had abdominal symptoms of various degrees of severity. When such symptoms arise a secondary gastro-jejunostomy may be recommended, although it is not certain that the operation will give relief, for the symptoms may be due to adhesions, in some cases at least. Mr. Crisp English (*Med.-Chir. Trans.*, 1903, vol. lxxvii.) found that only four out of fifteen cases had any gastric symptoms following the operation of closing the ulcer. These patients had symptoms of dyspepsia, for which two were readmitted into St. George's Hospital. Mr. Paterson (*loc. cit.*) traced thirty-three cases, and found that sixteen were quite well, but that seventeen suffered from gastric symptoms, and one of them died of a secondary perforation; two required gastro-jejunostomy as a

secondary operation, and nine had symptoms of gastric ulcer, and five suffered from dyspepsia. In two others, for which a primary gastro-jejunostomy had been performed, no symptoms were complained of within fifteen months and two years respectively. Paterson states that in one hundred and twelve cases collected from the statistics of two London hospitals there were thirteen deaths, which might possibly have been prevented by a primary gastro-jejunostomy; three died from hæmorrhage; in eight the sutures closing the ulcer gave way, and this led to secondary extravasation and death; and two died because a second perforation remained undiscovered in each of them. Mr. Moynihan has performed gastro-jejunostomy in six of these cases of perforated gastric ulcer, with five recoveries (*Med.-Chir. Trans.*, November, 1906).

THE CHOICE OF OPERATION.

Before discussing the relative merits of the chief operations now in vogue, it is important to draw attention to certain points which, in addition to careful asepsis, are essential to the success of all of them.

1. The anastomotic opening must be a large one, at least two and a half to three inches long, and half an inch broad, for otherwise it may contract, or even become closed, especially when the pylorus is not severely or only temporarily obstructed, as in certain cases of ulceration in the pre-pyloric region.

2. The orifice must be placed at the lowest part of the stomach as the patient stands, for most of the food has to pass through during the day. There is abundant evidence to show that vomiting and recurrence of symptoms are largely due to malposition and insufficient size and patency of the orifice.

3. Some of the mucous membranes of the stomach and jejunum should be excised in order to prevent obstruction of the opening by valves of mucous membrane. An elliptical opening is made instead of a mere slit (Littlewood and Moynihan).

When the Murphy button is used it is not necessary to excise any of the mucosa, for the button induces sufficient sloughing,

but the size of the aperture made by a button, which must be small enough to travel through the ileum, is too small for satisfactory and permanent drainage of the stomach; moreover, it heals by granulation, and is, therefore, unusually liable to contract.

4. *The use of clamps.*—Long, slightly-curved clamp-forceps are invaluable for this operation, for they :—

1. Prevent hæmorrhage.
2. Make leakage impossible during the operation.
3. Steady the parts during the operation and keep them outside the abdomen, where they are easily isolated by gauze packs so that contamination of the wound or peritoneum may not occur.
4. They also greatly facilitate the suturing, and prevent purse-string contraction of the orifice.

Doyen, Guinard, and other continental surgeons, were using clamps for this operation towards the end of the last century. Lane, Littlewood and Moynihan were amongst the first to recommend them in this country, and Mr. Moynihan's writings have done much to popularise them here and in America. Now their undoubted value is almost generally recognised; in fact, I consider them indispensable for the proper and safe performance of the operation. That I have had no death, so far, is very largely due to my adoption of the clamps from the beginning. The absence of a fatality during my greatest inexperience strongly recommends the clamps, especially as I have not confined myself to any one method of operating in other respects, and have only used the most perfect method of Mayo (*vide* p. 203) in my last eight cases.

Sutures.—It is best to use a continuous suture of reliable catgut, which pierces all the coats, and to reinforce this by a continuous sero-muscular suture of fine silk, or Pagenstecher's thread. It is essential for the deep suture to pierce all the coats, so that it may not bite out and lead to disastrous leakage before firm union has occurred. The continuous suture is far more quickly applied than interrupted stitches, and a continuous piercing suture controls hæmorrhage better than any other

available means; for this purpose the turns should not be more than one-eighth of an inch apart, and the thread must be kept taut throughout. Catgut, being absorbable, leads to less ulceration of the margins of the orifice than does silk or Pagenstecher's thread, which may take a long time to separate and get discharged into the intestine. Halsted's suture, although it is the most secure of the sero-muscular stitches, does not control hæmorrhage well, and several deaths from bleeding have followed its use; moreover, it is not so secure and lasting as a piercing suture, and as it does not bring the mucous edges together properly it is very apt to be followed by the formation of valvular folds of mucous membrane, which may obstruct the opening, unless this is unusually large. The deep suture may be either a circular (overstitch) or a mattress one; the former can be inserted most easily and rapidly, the latter is apt to cause puckering unless carefully applied, but it is useful to secure inversion towards the end of the circle. In either case the knots should be upon the mucous surface, for leakage is less likely to take place than if the knots are tied upon the peritoneal surface; but this risk is not so great here as in entero-anastomoses, for more serous approximation can be obtained here by the superficial suture without risk of obstruction by valve formation.

The continuous Lembert or Cushing suture should be used to reinforce the deep one, and it should turn in a little more of serous surface of the stomach than of the jejunum, so that the lumen of the latter may not be unduly narrowed or "flattened" against the stomach. Cushing's suture can be more rapidly applied than any other, and as it buries itself, fewer adhesions are likely to follow its use.

CHIEF OPERATIONS.

1. Posterior gastro-jejunostomy without a loop.
 - (a.) With dislocation and reversion of the direction of the jejunum.
 - (b.) Without dislocation and without reversion.
2. Anterior gastro-jejunostomy.
3. Posterior gastro-jejunostomy with a loop and with reversion.

4. Roux's "Y" method.
5. Anterior and posterior loop operations with entero-anastomosis.
6. Operations with the insertion of mechanical appliances.
7. McGraw's elastic ligature method.

It is not yet certain which of the many methods adopted at the present time is the best, and it is possible that better ways will be invented yet.

First an attempt will be made to compare *the merits and demerits of the anterior and posterior operations*. This is necessary, because a few surgeons' still strongly recommend the anterior operation.

1. *Anatomical and physiological considerations*.—If drainage of the stomach depends to any great extent upon gravity, it is clearly best to make the opening low down upon the postero-inferior surface (*vide* Fig. 1). This is true even when the body is upright, and still more so when the patient is recumbent. But the weight of the long limbs of the jejunal loop, which is used for the anterior operation, certainly does drag the anterior opening downwards to some extent in time. It must be remembered also that the stomach is not a passive bag, and that its drainage is not entirely dependent upon the force of gravity. The larger the stoma, however, and the more damaged the muscular power of the stomach, the greater the advantage of securing a dependent opening upon the posterior surface. The results of the ingenious experiments of Cannon and Blake upon healthy stomachs are not strictly applicable to the diseased conditions which call for gastro-jejunostomy.

Physiologically it is an advantage to make the opening high up in the jejunum, so that as little as possible of the small intestine may be lost for digestion and absorption, but the researches of Paterson tend to show that absorption is not seriously interfered with by anterior gastro-jejunostomy in which the opening into the jejunum is lowest. It is of more importance to prevent the acid chyme from reaching the jejunum too low down, and un-neutralised by the bile and pancreatic juice.

¹ Vide Mr. Paterson's Hunterian Lectures, *Lancet*, vol i., 1906.

Gastro-jejunostomy.

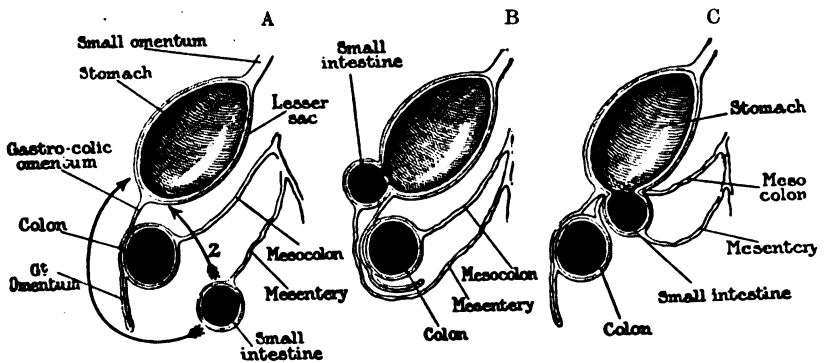


Fig. 1.

Diagrammatic sagittal sections illustrating the normal relations of the parts concerned in gastro-jejunostomy. A shows the anatomical relations before operation, the patient being in the erect position. B and C demonstrate how unfavourably the anterior operation (B) compares with the posterior (C), even when the body is erect. When the patient is supine, the anterior opening is still less effectual, as can be seen by turning this page on its right side. (Greatly modified from Von Esmarch and Kowalsig.)

Therefore, upon anatomical and physiological grounds, the posterior operation without a loop is better than any anterior operation, and it is more than probable that the posterior no-loop operation, without dislocation and without reversion of the jejunum, is better than all others, because it interferes less with the normal anatomical and physiological relations and conditions. If anyone should still prefer to use a Murphy button, the posterior operation is the best to choose for it, because it falls into the stomach in at least a third of the anterior operations, whereas it is retained in the stomach after only about one-tenth of the posterior operations.

2. The anterior operation may be a little easier, more rapid, and need cause less exposure of the viscera, and perhaps less shock than the posterior "no-loop" operation, especially if performed by surgeons of little experience and skill; but the difference is small, and the time saved is trivial, for most of the time consumed in either operation is spent in making the actual anastomosis.

A short or diseased meso-colon may occasionally make the posterior operation difficult, or even impossible, and adhesions of the posterior wall of the stomach may very rarely do the same, but it is exceptional for either growth or simple ulceration to affect the part of the stomach which is incised for posterior gastro-jejunostomy. When this part is affected by growth, it is generally too late for the operation to be performed at all. A bulky great omentum may occasionally prolong and increase the difficulties of anterior gastro-jejunostomy.

Posterior no-loop operations with the aid of clamps are little, if any, more difficult than either the anterior or posterior loop operations. Personally I have not found the posterior no-loop operation without reversion of the jejunum to be more difficult than the loop operation. It has been stated that the jejunum may limit the mobility of the stomach in "no-loop" operations, but there is as yet no real evidence of the validity of this theoretical objection. In one case, in which the jejunum originated to the right of the spine, Munford (*Annals of Surgery*, 1906, vol. xliii., p. 88) unfortunately performed the operation

without a loop, with the result that the excessive tension led to separation and leakage at the suture line, but this rare case was probably unsuitable for this operation.

3. *Severe vomiting* (so-called "vicious circle.")—The evidence upon this point appears to be somewhat conflicting. Dr. Ticehurst collected ninety-eight Guy's Hospital cases for his able thesis, which has been of great help to me. His cases and conclusions are of especial value, because the operations were performed by *many different surgeons*, between January, 1899, and June, 1905, so that the facts and conclusions are not gathered from the published accounts of a series of operations by any one surgeon, which are too often misleading. In ninety-eight consecutive operations at Guy's Hospital, the anterior method was chosen twenty-four times; out of ten cases of serious vomiting seven followed the anterior operation (with four deaths), whereas this complication followed only three of the seventy-four of the posterior operations.

Mayo, on the other hand, states that "vicious circle" occurred most commonly after the posterior loop method, owing to the liability of the comparatively short loop to kink. In fifty-three of these operations there were three deaths; the primary result was good in the remaining fifty, but seven required a secondary operation for gradually developing symptoms of obstruction, with regurgitation of bile, etc.

The truth seems to be, that acute serious vomiting is more likely to follow the anterior operation, and chronic or gradually developing vomiting is more common after the posterior operation with a loop. So far as the evidence goes, vomiting is rarer after the posterior "no-loop" operation than after any other method except that of Roux, which is too severe and tedious for general adoption. This and entero-anastomosis will be briefly discussed later.

It is certain that vomiting is less common when the opening is made within three inches of the origin of the jejunum than when it is made lower down, so that a loop of proximal jejunum hangs down from the anastomosis. It is probable that vomiting will be least common after Mayo's operation, in which no loop is formed

and no reversion of the direction of the jejunum is made (*vide infra*). Mayo states that no death and no trouble followed in any of sixty-three cases operated upon by this method since July, 1905.

5. *Intestinal obstruction*.—This has been a little more frequent after the posterior operation. Moynihan (*Lancet*, 1906, vol. i., p. 1345) mentions three cases in which the small intestine herniated into the lesser sac through the rent in the meso-colon. This accident should not occur again, for it can be prevented by carefully sewing the edges of the rent to the jejunum or stomach. This orifice has also contracted upon the jejunum or upon the anastomosis, but this rare event is probably preventable by careful suturing, as above indicated, and by lessening the formation of adhesions by clean and aseptic work. After the anterior operation, the jejunal loop has compressed the colon, or *vice versâ*, and, in one of the Guy's Hospital series, both the jejunum and the colon were obstructed by mutual compression, although the anastomosis was made twenty-four inches below the duodeno-jejunal flexure: the obstruction was so complete that the intestine between the jejunal loop and the middle of the transverse colon was collapsed and almost empty. In one case, quoted by Mayo, the small intestine passed over the afferent jejunum and became strangulated. Intestinal obstruction is very unlikely to follow the posterior operation without the formation of a loop, and there is no instance on record, as far as I know.

6. *Mortality*.—The death-rate has been much higher after the anterior operation, but this may be partly due to the almost exclusive adoption of this method in the early days of the operation, before experience and skill were acquired, and partly to its selection in grave cases with the mistaken object of saving time. In nineteen *malignant cases* recorded by Ticehurst, the anterior operation had a mortality of 53 per cent., whereas in thirty-one posterior operations for *malignant disease* the death-rate was 35 per cent. A similar comparison of the operations for pyloric stenosis of benign origin affords even more conclusive evidence in favour of the posterior operation. Dr. Murphy,

Dr. Mayo, and most other authorities agree that the mortality of the anterior operation has been higher in the past. The great improvements which have lately been made in the posterior operation have decreased its mortality so much that there can be no doubt that this operation now carries less risk of death than the anterior operation.

7. *Perforating jejunal ulcer*.—This has been far more frequent after the anterior operation, and especially after adding entero-anastomosis to any form of gastro-jejunosotomy. Moynihan (*Lancet*, 1906, vol. i., p. 705) mentions thirty-three cases, in twenty-nine of which the nature of the operation is recorded. This grave complication followed seventeen anterior operations, four anterior with entero-anastomosis, one anterior “Y” operation (Roux), and six posterior loop operations with entero-anastomosis. Its occurrence seems to be chiefly due to the action of the over-acid chyme upon the jejunum, and especially to its action upon the part of the jejunum which is between the stomach and the intestinal anastomosis. In the cases in which this plan is adopted, bile and pancreatic juice are not able to reach this part to neutralise the acid which is poured out from the stomach.

Paterson (*loc. cit.*) thinks that it also indicates unsatisfactory drainage of the stomach, for hyperchloridria ought not to occur with efficient drainage.

The risk of this complication is a strong argument against the adoption of the anterior operation, and especially against the operations which need entero-anastomosis to make them safe from “vicious circle.”

It must not be forgotten that all the jejunal peptic ulcers do not necessarily perforate, but many of them may persist and be the cause of chronic dyspepsia.

8. Posterior operations allow a more thorough examination of the posterior wall of the stomach.

In conclusion, it seems to me that the improved posterior operation (*vide infra*) is very much to be preferred to any kind of anterior gastro-jejunosotomy.

Next, a few remarks will be made upon some of the complicated operations.

(a.) Roux's "Y" method was invented with the object of preventing "vicious circle," and it is no doubt one of the most certain methods of attaining this object, but the chief objections to this operation are:—

1. That the two anastomosis make the operation more complicated and prolonged, so that it is not suitable for grave cases or for routine use.

2. Now that "regurgitant" vomiting is known to be preventable by simpler means, and effectual drainage can be provided by means of a large opening suitably placed, it is no longer necessary to use Roux's more tedious and serious method.

3. The danger of peptic jejunal ulcer is increased because several inches of the jejunum are exposed to the action of the acid of the gastric juice, without the neutralising effects of the bile and pancreatic juice (Paterson). In malignant disease this objection does not hold, for jejunal ulcer has not yet been known to follow gastro-jejunostomy for malignant disease (Moynihan, *Lancet*, 1906, vol. i., p. 1071).

(b) *Gastro-jejunostomy with entero-anastomosis*.—This is a simpler but less effectual method, which has been designed for the same purposes as Roux's operation, and it has the same objections.

Secondary entero-anastomosis has often been resorted to for vomiting coming on either early or late after loop operations, and it has generally, but not always, proved successful. It should be rarely required at the present day, and this is also true of the complicated operations of Doyen and others which involve occlusion or partial occlusion of the proximal part of the jejunum or of the pylorus.

THE MURPHY BUTTON.

Some criticisms of the "*ingenious*" methods may be made here. A button which is small enough to travel safely through the ileum is not large enough to make a satisfactory and permanent gastro-jejunostomy, except possibly in cases of very severe and permanent obstruction of the pylorus.

Paterson, in his Hunterian Lectures, mentions three cases in which the fistula had completely closed after intervals of three and five months, and two complete closures were seen to have occurred in sixty-nine of the cases collected by Dr. Ticehurst.

The button may be retained, and may act as a foreign body either in the stomach or intestine. Mayo mentions two cases in which it had to be removed from the stomach. Dr. Hawkins and Mr. Nitch record another case in which the button caused intestinal obstruction, which was fortunately relieved by the removal of the button by operation (Trans. Royal Medico-Chir. Soc., Nov. 1906).

Dr. Ticehurst points out that the button may pass the right way, or it may enter the stomach or the proximal loop, eventually reaching the duodenum in some cases. In nine cases of his collection it was known to have been retained in the stomach, and not one of these patients obtained any permanent relief from the operation.

Hildebrand and Weir have modified the button, with the object of preventing its retention in the stomach, but no modification can be relied upon to prevent the button falling into the stomach in the anterior operations.

The brothers Mayo (Annals of Surgery, 1905, vol. xlii., p. 546), in fifty-seven cases, had four deaths from separation at the line of union between the sixth and the tenth day. Since then they have reinforced the anastomosis by mattress sutures. This leakage from sloughing after some days has been a common experience; three out of twenty-three deaths in Ticehurst's collection were due to this cause, and in one of these a perforation had also occurred over the prominent rim of the button.

It has been claimed that the button is one of the simplest of all the methods of performing gastro-jejunostomy, and this is certainly true, but it is also the most dangerous method for skilful surgeons to adopt, although it may be the safest for those who have no skill in suturing, and no just appreciation of the details of technique, which are necessary for the more perfect suture operation.

The button has been frequently used in order to save time in grave, and especially in malignant, cases, but these are just the patients for which the button is least to be recommended, for it sloughs out rapidly from their ill-nourished tissues, which are incapable of quick plastic repair. No one can foretell where the sloughing may cease. The button is least objectionable when used in the posterior no-loop operation, and reinforced by mattress sero-muscular sutures. Czerny has had great immediate success with this method.

The elastic ligature method" is a very simple and rapid one, which carries less risk of shock and sepsis than any other method, but it has the serious disadvantage of not providing an immediate opening, so that mouth feeding may have to be delayed for about four days in cases of pyloric obstruction. Therefore it is not suitable for this condition, for much of the success of the present day is due to early feeding in these patients. Occasionally the ligature may break before it has made an opening, or it may fail to bite out. Personally I prefer to adopt the direct suture method, leaving nothing to chance or to sloughing.

POSTERIOR 'GASTRO-JEJUNOSTOMY.

Posterior gastro-jejunostomy has been very considerably modified in recent years. Many of the modifications have been too complicated and unsatisfactory for general adoption, but it has been proved to be a great advantage to make the anastomosis within three inches of the origin of the jejunum, instead of lower down. It is of no advantage to have a loop of jejunum hanging down between the duodenum and the anastomosis, and experience has amply proved that this loop adds greatly to the risk of "vicious circle." Czerny performed the operation without a loop years ago, generally with the aid of the button and supplementary sutures, with great success.

Dr. Rogers states that this operation had been performed 215 times for benign cases in Czerny's clinic, with only ten deaths (Annals of Surgery, vol. xxxix., p. 512). It is not stated what the

* Operations of Surgery, vol. ii., p. 521.

late results were like, but I should judge, from what I know of the late results of other cases, that return of symptoms probably occurred in some of them, due to narrowing or occlusion of the small orifice made. The advantages of dispensing with a loop have become widely known from the writings of Petersen, and the operation has been made much easier and safer by the aid of clamps, which have also allowed us to make a much larger opening. Until lately it has been customary to reverse the natural direction of the jejunum before attaching it to the stomach, because it was believed that it was essential for the direction of peristalsis to be the same in the stomach and the attached jejunum. Mr. Moynihan has used the "no-loop" with reversion method in a great many cases, without any trouble, and recommends it in his work on "Abdominal Surgery" (1906).

Dr. W. J. Mayo (Annals of Surgery, vol. xliii., p. 537) has, however, published two cases in which chronic bile regurgitation of a serious character developed. In each of these "the occasional regurgitation of quantities of biliary and pancreatic secretions was a source of discomfort and considerable disability. Re-operation in both cases, during the past summer (1905), showed that the cause of trouble was an angulation of the jejunum at its gastric attachment."

These troublesome complications followed two out of fifty-six "no-loop with reversion" operations performed between January 1st and July 1st, 1905, with only one death.

These cases led Dr. Mayo to doubt whether it was really necessary to reverse the direction of the jejunum. Normally the jejunum ascends a little from its origin towards the left, and then falls downwards, backwards and to the left towards the front of the left kidney. When it is fixed to the stomach in the usual way, it is rotated and dislocated to the right, so that kinking may possibly occur at the anastomosis, and the distal part of the bowel rides forward and to the right over the prominence of the lumbar spine. The shorter the loop the more likely the kinking. The brothers Mayo were unable to find any valid reason for reversing the normal direction of the jejunum in the "no-loop" operation, and they have, therefore, discarded it. Now they perform the

anastomosis without permanently disturbing the natural relations of the parts, and in the last sixty-three cases they have had no death and no trouble of any kind.

These results are very good, and the theoretical advantages of the operation are so obvious that I have used the method in eight cases. The results have been so much better than the average that I believe the operation deserves to be better known and thoroughly tried. Now that we know that "vicious circle" is nearly, if not always, due to the unsatisfactory position and size of the stoma, there does not seem to be any reason for rotating and dislocating the jejunum, which probably drains the stomach better when it is left in its natural position.

Posterior gastro-jejunostomy without a loop and without reversion or dislocation of the jejunum.—(Mayo.)

The operation which I am about to describe is that of Dr. Mayo, with slight modifications. The method of suturing is only a modification of that described by Mr. Moynihan.

The patient is kept in bed for two or three days and thoroughly prepared. The mouth and teeth are thoroughly and regularly cleansed, the bowels are kept open, the stomach is washed out if its contents are foul, and nothing but sterile milk is given for two days before the operation. The abdomen is shaved and compressed over night.

A vertical incision four inches long is made half an inch to the right of the middle line over the upper part of the rectus abdominis, and extending down to the level of the umbilicus. When operating for irremovable malignant disease it is an advantage to make the incision through the left rectus, for this enables us to make the gastric incision as far as possible to the left and well away from the growth, so that the opening may keep patent as long as possible. The rectus sheath is exposed and opened. The outer margin of the incision is raised from the muscle for a quarter of an inch, so that it may be used to overlap the inner margin later on, after Noble's method for the prevention of ventral hernia.

The muscular fibres of the rectus are separated and the posterior wall of the rectus sheath and the peritoneum are

incised together in the line of muscular separation. No attempt is made to place the deep part of the incision under cover of the rectus muscle, for this makes suturing very difficult, especially in muscular subjects.

The stomach and first part of the duodenum are thoroughly examined before deciding which operation, if any, to perform.

The great omentum and transverse colon are drawn well forwards, upwards and to the right, making the meso-colon taut, and bringing it well into view.

A bloodless part of it is selected, picked up with tissue-forceps, drawn downwards away from the stomach and snipped with scissors. The opening thus made into the lesser sac is carefully enlarged until it admits three fingers. The opening is made within the vascular arch formed by the middle colic and ascending branch of the left colic arteries, great care being taken to select the proper interspace. Its direction is downwards, forwards and to the left, when the meso-colon is returned to its natural position. This direction is selected because it corresponds to the normal direction of the part of the jejunum which is joined to the stomach (*vide* Fig. 2) and to the long axis of the incision in the latter (*vide* Figs. 2, 3 and 4). In this way kinking is avoided when the jejunum is attached to the sides of the aperture in the meso-colon, after the anastomosis has been completed.

The posterior surface of the stomach is thoroughly examined. The part of the greater curvature which lies lowest in the abdomen is selected for the site of the anastomosis. Mayo places his incision almost vertically below the cardiac orifice, well to the left of the more muscular pyloric third of the stomach (Fig. 2). In malignant cases the opening is made as far to the left as possible. When the proper site has been noted, the left hand is used to push the posterior wall of the stomach through the rent in the meso-colon, care being taken to expose the actual lower border of the stomach, and about a quarter of an inch of the anterior surface also, by carefully displacing the gastro-colic omentum to the required extent (Fig. 3).

Long curved clamps, sheathed in rubber, are then placed obliquely with their handles directed towards the left shoulder.

Gastro-jejunostomy.

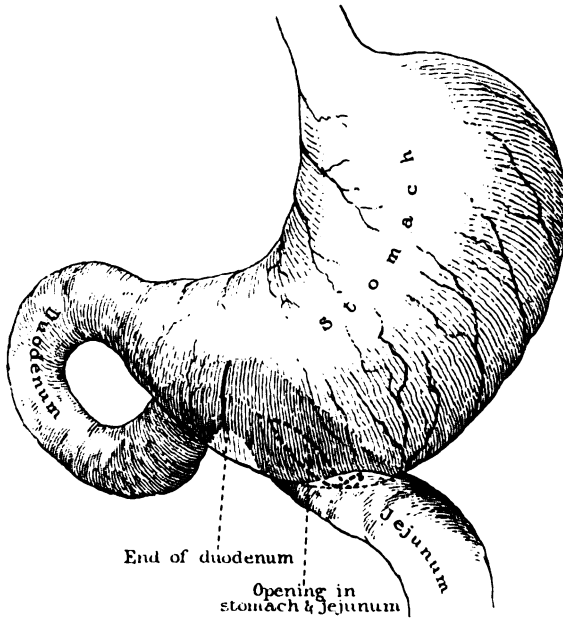


Fig. 2.

Posterior gastro-jejunostomy without a loop and without reversion of the jejunum. (Modified from Mayo, *Annals of Surgery*.) The anastomotic opening is about three inches long, and extends to the anterior surface of the stomach. Its upper end is within two inches of the duodeno-jejunal flexure.

Gastro-jejunostomy.

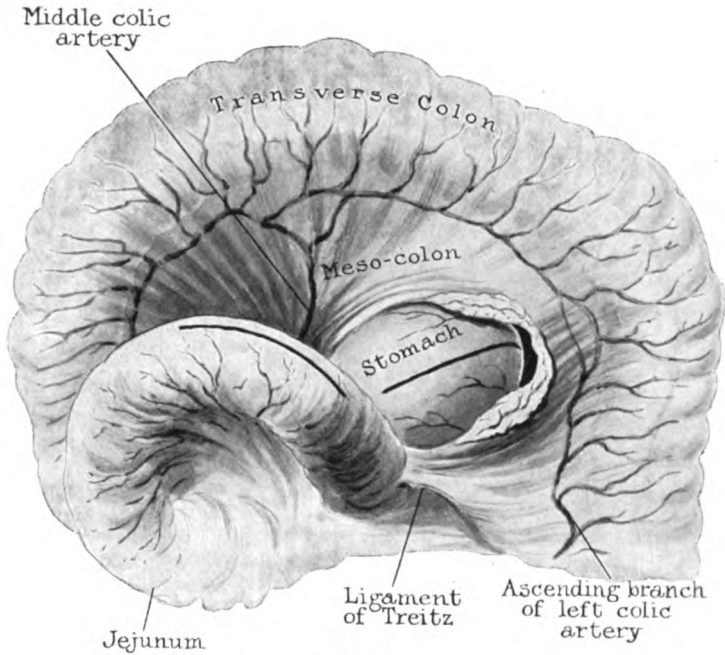


Fig. 3.

Posterior gastro-jejunostomy without a loop and without reversion of the jejunum. An oblique opening is made through the meso-colon towards the left and between the meso-colic and ascending branch of the left colic artery. The black line upon the posterior wall and lower border of the stomach indicates the site of the opening. The great omentum is separated from the greater curvature for a short distance, to allow the anastomosis to extend a little in front of it. The site of the opening into the jejunum is also shown. The bowel is only displaced to the right for diagrammatic purposes (*vide* Fig. 4).

Gastro-jejunostomy.

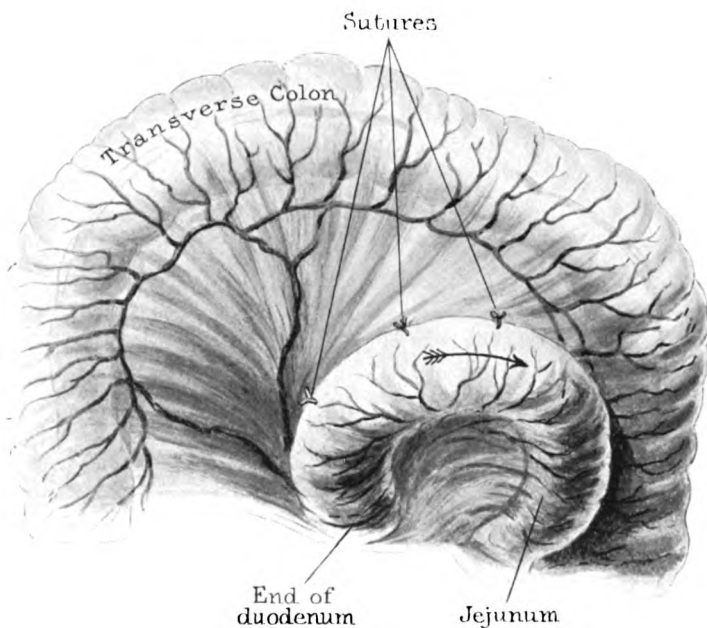


Fig. 4.

Posterior gastro-jejunostomy without a loop and without reversion of the jejunum. The anastomosis has been completed, and the jejunum sutured to the meso-colon, so as to prevent an internal hernia through the rent in the latter. This operation involves less change of the natural relations of the viscera than any other.

The bases of the blades meet in front of the lowest point of the greater curvature. The fold of stomach drawn into the clamp and emptied should be at least four inches long and two inches broad. By drawing the transverse colon forward and to the right, and passing the finger backwards and to the left along the under-surface of the meso-colon, the duodeno jejunal flexure is easily found. The flexure and the ligament of Treitz, which attaches it to the root of the meso-colon, should be actually seen to prevent any mistake (Fig. 8).

The jejunum near its origin is brought out of the wound and emptied by drawing it through the fingers. It is not rotated to the right. A fold of it four inches long, including the free border, is clamped, the tips of the blades being about one and a-half inches from the duodeno-jejunal flexure. It is easier to place the clamps (with their handles to the left), when the bowel is not reversed, so that the operation is facilitated by avoiding reversion. It is always an advantage to have the handles to the left when the assistant who holds them stands on that side of the patient. Special self-retaining clamps can be procured, but some of those sold have blades which are too pliable, so that the points of the *gastric* clamps gape and have to be tied together to avoid retraction and hæmorrhage.

The protruding portion of the omentum, colon and excess of jejunum, are now returned into the abdomen to avoid any possible contamination during the next stages. With the same object a gauze pack is placed just below the meso-colon in the abdomen, and a roll of gauze moistened with hot normal saline is placed between the two clamps, which are then closely approximated and held in apposition by an assistant. Moist packs are carefully applied all around and under the clamps, so that the pouches of stomach and jejunum are isolated. Moist packs are more efficient than dry ones, for they cling and lie better.

A continuous sero-muscular suture of Pagenstecher's thread, or fine silk, is now used to join the adjacent edges of the two pouches for a distance of four inches. It is begun on the left, where the tail thread of the knot is held with forceps. The thread is always held taut, to secure close apposition and to raise

a fold of sero-muscular tissue after each stitch; this simplifies the introduction of the next one.

When the first half of the circle of superficial suture has been made, the needle is laid aside, and the serous and muscular coats of the stomach and jejunum are carefully incised, for three inches, so as to expose the mucous membranes, which pout into the wounds. An elliptical piece of mucosa, about three inches long and about half an inch wide, is excised from the stomach and jejunum. The incisions should be a quarter of an inch in front of and parallel to the posterior sero-muscular suture line. Reliable catgut is chosen for the deep suture, which must pierce all the coats, and is commenced at the left extremity of the wound, and continued as a circular or overstitch as long as inversion of the edges can be easily made.

Retraction of the gastric mucous membrane is prevented by the careful insertion of the first sutures, and by means of tissue forceps, which pick up all the coats of the stomach and jejunum, and are placed at the right extremities of the wounds and close to their edges, where they do no harm. As soon as difficulty arises in securing inversion of the edges, the needle is passed after Connell's method. This is an excellent and rapid way of completing the suture. Both knots should be placed upon the mucous surface.

Care must be taken to keep the thread always taut, and the turns should not be more than one-eighth of an inch apart. These precautions secure accurate apposition of the mucous membranes and, especially, prevent hæmorrhage. The jejunal clamp is now removed, but the gastric one is left on, so that it may retain the parts in the wound during the completion of the sero-muscular suture, which is rapidly done after the method of Cushing. The whole circle of union is examined, and, if necessary, a reinforcing suture may be placed at any weak spot.

The parts are cleansed with swabs moistened with saline solution, and the packs are removed. The transverse colon is brought out again and drawn forward so as to expose the rent in the mesentery to enable the surgeon to fix its margins to the jejunum or stomach. Failure to do this well may lead to the

formation of an internal hernia. I have operated upon one patient in whom the anastomosed loop of jejunum had been drawn up into the lesser sac and had become constricted by the contraction of the meso-colic incision and the formation of adhesions. An eight-inch loop had been used at the primary operation, and no attempt had been made to close the meso-colic opening with sutures. Four sutures are sufficient, one in front, one behind, and one at each side. Mayo uses mattress stitches, which are passed in such a manner that they turn the raw edges of the rent upwards towards the lesser sac, so as to lessen the risk of adhesions. As advocated by Moynihan, it is better to sew the edges to the jejunum than to the stomach. This plan is easier, and helps to fix the jejunum in a good position (Fig. 4). The viscera are replaced and the abdominal incision closed, the anterior rectus sheath being overlapped as recommended by Winslow and Noble. Catgut is used for the fascial suture, and Pagenstecher's thread for the peritoneum and deep layer of the rectus sheath.

AFTER-TREATMENT.

A saline enema is given soon after the patient has returned to bed. Unless there is unusual collapse, the semi-sitting attitude of Fowler is adopted as soon as the patient has come round from the anæsthetic. This facilitates the drainage of the stomach and prevents the contents of the small intestine from flowing into the stomach. Gastric juice, mucus, blood and any bile and pancreatic juice that may reach the stomach, drain away through the anastomotic opening, which lies at the lowest part of the stomach when this position is maintained; vomiting is thus avoided. Moreover, the lungs have freer play and a better circulation, so that pneumonia and other pulmonary complications are less likely to develop.

If shock is severe, as it may be in late cases or malignant disease, this is combated as usual by warmth, saline rectal infusions, and subcutaneous injections of ernutin *m*x. every four hours. Nutrient enemata are avoided as far as possible, for mouth-feeding is far preferable and more nutritious. For the

first five hours, only water is given by the mouth, and then 5x. feeds of milk and barley-water, and albumen water, are given every hour at first, and the feeds are gradually increased, and given at longer intervals. Iced whipped eggs are also given after Lénhartz's method; and after twenty-four hours, jelly, flavoured in various ways, is given, and the amount of milk rapidly diminished, because of the flatulence which it induces.

Albuminous foods are better than farinaceous after this operation, for the former combine with and neutralise the acid of the gastric juice and prevent its harmful action upon the damaged and sutured tissues. Moreover, proteids are more nutritious and less bulky. Unless there is active ulceration in the stomach itself, fish and chicken are given by the end of a week.

Patients with duodenal ulceration seem to be able to stand full diet earlier than the subjects of prepyloric or gastric ulceration, and it is probable that this clinical observation is accounted for by the efficiency of the large anastomotic opening which is now made. One of my patients had not eaten any solid food for nine months except on one or two occasions, when he had tried toast, which gave rise to agonising pain. Within a week of his gastro-jejunostomy he was taking fish and other solids without any discomfort, yet he had no stenosis of the pylorus, but a large duodenal ulcer, which had caused jaundice on several occasions by interference with the bile-duct or biliary pupella. It must be remembered, however, that when there is an open ulcer, either in the stomach or duodenum, time and rest are required for healing, and that such patients are not fit to return to work for at least three months after the operation. They need feeding up and rest of body and mind. Their nutrition, both local and general, usually improves with remarkable rapidity, because of their ability to take plenty of food after suffering from pain and semi-starvation or chronic hæmorrhage for months or years. The improvement may be so great that both the surgeon and the patient may be deceived, and led to believe that the ulcer has healed. In such cases premature return to the battle of life may do much harm and cause a return of symptoms.

(Read before the Obstetrical Society, July, 1907.)

PRIMARY EMBOLIC CHORION- EPITHELIOMA OF THE VAGINA.

By HENRY THOMAS HICKS, F.R.C.S. ENG.

PRIMARY chorion-epithelioma of the vagina is of such great interest and the recorded cases so few that I venture to bring this case before the Society, hoping it may help to throw some light on this rare condition.

E. J—, aged 28, was admitted into Guy's Hospital on July 10th, 1906, for pain in the left chest and dyspnoea.

Previous history.—The patient was married and had had three children and no miscarriages, and had always had good health up to the present illness. Menstruation had been regular and normal in amount up to seven months before admission, since which time she has had amenorrhœa.

On June 21st she was taken ill with shivering and was found to have left basal pneumonia. The next day she began to bleed from the uterus, and her medical attendant sent for the assistance of the obstetric resident at Guy's Hospital. The cervix was dilated and a large hydatid mole, together with a 5½ months dead, but fresh, foetus, was cleared out of the uterine cavity. Dr. Crofts, the obstetric resident, gave the following description of the uterine contents:

“There was a foetus about the age of 5½ months, born dead, but in quite a fresh state and enclosed in the

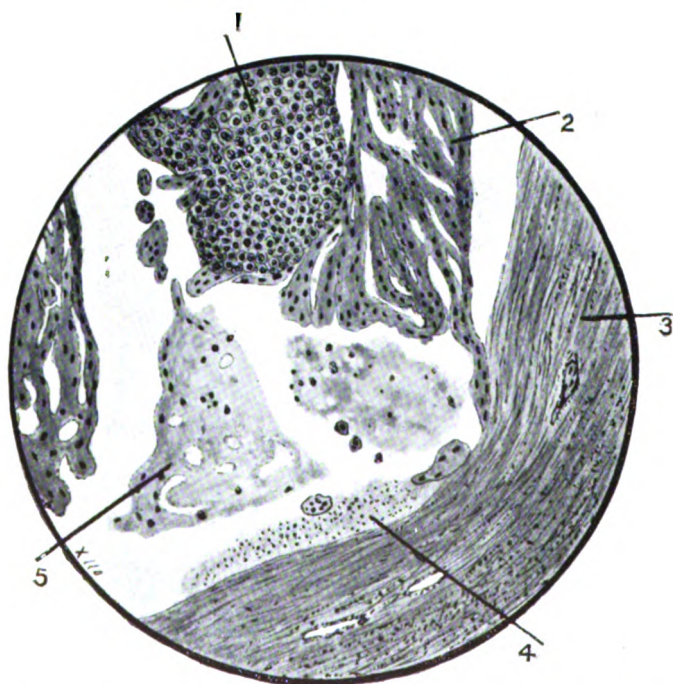
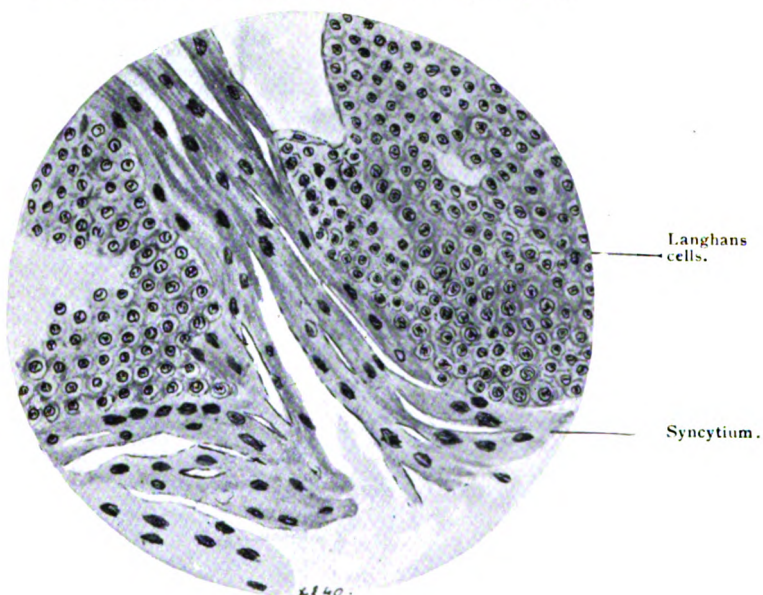
amnion. That part of the placenta to which the cord was attached appeared to be normal, but around the periphery of this normal patch of placenta and all over the general aspect of the chorion there was a marked vesicular formation, which, taken as a whole, formed a large vesicular mole. After clearing out, the uterine cavity was found to be smooth but soft, and there was no evidence in favour of twin pregnancy."

The dyspnœa and pyrexia continued and the patient was admitted into Guy's Hospital under the care of Dr. Taylor. Empyema was diagnosed and drained. The temperature, however, rose at night for some weeks after the operation, and Dr. Taylor thought that the pelvic trouble might possibly be the cause of the continuous pyrexia.

I saw the patient on July 20th, and found no evidence of pelvic inflammation. There was a blood-stained discharge of dark venous colour which the patient said had been present since the miscarriage in June. The bleeding was not profuse, nor did it increase on examination. The uterus was soft and bulky, giving one the impression that involution had been interfered with. The pyrexia had existed for nearly a month and sub-involution was likely. There was a soft single cyst high up in the left fornix of the vagina of about the size of a big Tangerine orange, and below, on the posterior wall of the vagina about two inches from the vulva, was a small knob about the size of a cob-nut. The upper soft cystic swelling seemed to be a superficial vaginal cyst and was covered with unaltered vaginal mucous membrane. The lower swelling was soft and looked bluish-purple beneath the vaginal mucous membrane.

The question of chorion-epithelioma was raised, and Dr. Taylor agreed to an exploration as soon as the condition of the empyema would allow of it. At first the patient did not progress very satisfactorily, owing to some difficulty in draining the pleural cavity, but the pelvic condition became no worse. There was some slight

Primary Embolic Chorion-epithelioma of Vagina.



1. Mass of Langhans' cells. 2. Syncytium. 3. Vaginal wall. 4. Blood and fibrin. 5. Degenerating mass of syncytium.

bleeding from the vagina during the next fortnight, and the lower swelling increased a little in size; the cyst remained unaltered. On August 20th an anæsthetic was given, and the small tumour, which about doubled in size, was removed from the vagina for examination. It was very vascular and some large vessels in the perivaginal tissues had to be underrun. The patient took the anæsthetic very badly. The tumour when removed was about the size of a small walnut, and when *in situ* formed a soft, well-defined swelling placed deeply in the perivaginal tissues close against the rectal wall, and covered on its vaginal aspect with normal mucous membrane. The sections show the normal squamous epithelium of the vagina supported by sub-mucous tissue. In the deeper parts of the vaginal walls are numerous spaces filled with a cellular growth. The cells are of two distinct varieties. There are patches of closely-packed cells; each cell has a clearly defined nucleus: these are Langhans's cells. Arranged around each pack of Langhans's cells large quantities of syncytium are seen. The syncytium is formed of large branching ribbons of multinuclear protoplasm staining deeply with eosin. In many places the protoplasm has undergone vacuolation, and the characteristic oblong nuclei of the syncytium are swollen and less deeply stained than those seen in the syncytium which has not become vacuolated.

Although as a rule the syncytium keeps to the periphery of each pack of Langhans's cells, in many places small pieces of irregular, multinuclear protoplasm are mixed up with the single nuclear cells. In the deeper parts of the sections the growth is more abundant, and here it is embedded in necrotic tissue and fibrin. There are no chorionic villi to be seen in any of the sections, but it is quite possible that degenerate villi may be hidden by the hæmorrhage and necrosis, which occurs in large areas. Many dilated venous spaces appear in the perivaginal tissues, and some of these are filled with masses of syncytium; the larger spaces contain small clumps of

Langhans's cells as well. It seems, therefore, that the growth spreads along the peri-vaginal venous spaces, and the syncytium, as it were, pilots the Langhans's cells along these paths.

September 2nd.—The patient seems very well. There is no bleeding, and the uterus is of normal size. The cyst in the left lateral fornix has disappeared spontaneously, but there is a small dimple at its original site.

September 26th.—As far as clinical examination goes the patient is quite free from growth.

October 24th.—Patient came to-day. There is no evidence of any growth. She has had two normal menstrual periods lasting four days on each occasion.

November 29th.—Patient well and putting on weight. There is no hæmorrhage other than a normal period, and the local condition seems in every way satisfactory.

December 23rd.—Examination was again negative.

Further history of the case.—Vagina remained free from growth until January 8th, 1907, when a small, soft, but well-defined tumour, of about the size of a walnut, was found in the lower part of the anterior vaginal wall. In five days the tumour almost doubled in size, and it was deemed necessary to remove it immediately.

The growth was situated deeply in the perivaginal tissues at the vaginal outlet. In front it bulged towards the vestibule to the right of the urethra, which was displaced forwards and to the left. It was covered on its vaginal aspect with normal rugose mucous membrane.

A transverse incision was made in front of the growth, and the urethra was separated off as high as the base of the bladder and upper limit of the tumour. The whole width of the lower half of the anterior vaginal wall was removed with the tumour. The growth was soft, friable, and hæmorrhagic. There was a thin, but definite capsule on its deep aspect, but at the periphery out-lying pockets of growth could be seen in the peri-vaginal tissues, especially on the right, and the vaginal wall was excised freely in consequence of this infiltration. The cut edges

of the vagina and the urethra were brought into position by catgut sutures. Six weeks later a soft peri-vaginal swelling appeared higher up in front and on the left, which seemed to have no connection with the previous tumour, and was covered with normal vaginal mucous membrane. It was about the size of a walnut and was also removed, but with considerable difficulty, owing to the close relationship of the bladder and the brisk hæmorrhage which occurred at its removal.

Within three weeks another tumour appeared in the posterior vaginal wall, below the site of the first tumour, and the cyst, which had disappeared in August last, refilled, and formed a soft swelling in the left lateral fornix. The cyst and growth were removed on March 16th, 1907. Some thickening was noted in front beneath the scars in the vaginal wall which was taken to be cicatricial and inflammatory tissue, but in a few days soft growth was found creeping forward along the vestibule to the right of the urethra, and on further examination a soft, diffuse infiltration was discovered in the peri-vaginal tissues high up on the left in front. There was now no definite tumour formation, but a soft growth spread along the peri-vaginal tissues in a most insidious manner rendering further operation hopeless. Up to the middle of April the patient's general condition remained good, and previous vaginal growths had given rise to no symptoms. The growth now began to increase rapidly, running forward to the clitoris, enlarging it to about the size of a walnut, and the peri-vaginal tissues in front became boggy and swollen by infiltrating growth. The patient did not waste much but became very anæmic, and complained of considerable local pain. Menstruation had been regular up till February last, since when there had been no loss of blood.

On April 19th hæmorrhage from the vagina set in for the first time, and the growth was found to be fungating through the vaginal mucous membrane on the left. The patient went rapidly downhill, and signs of broncho-pneumonia developed at the base of the right lung, which

was taken to be due to pulmonary metastases, but there was no hæmoptysis. The bleeding from the vagina recurred several times, was never severe, and no doubt much of the anæmia was due to hæmorrhage into the growth itself.

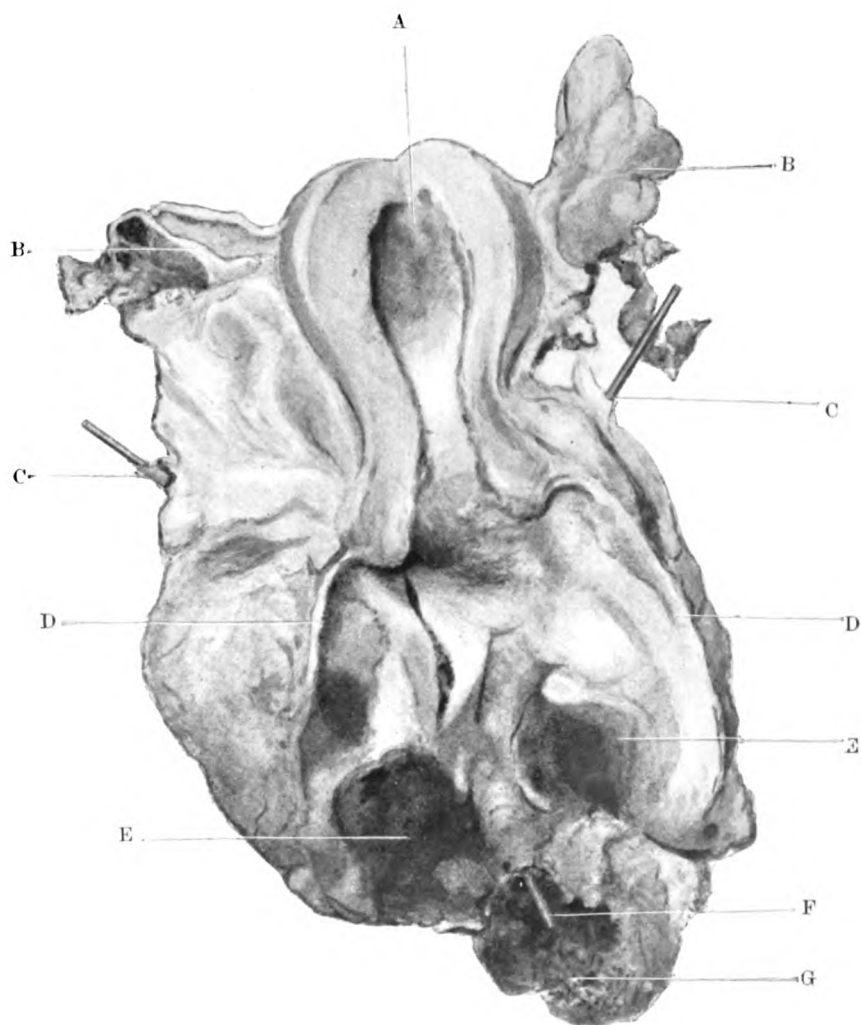
The patient died on May 8th, 1907, eleven months after the passage of the mole.

Report of the autopsy.—The body is not much wasted, but very pale. There are no secondary deposits in any of the organs except the right lung. The left lung is firmly adherent to the parietal pleura, the adhesions being the result of the old empyema. The left lung contains no growth. This might be explained by the hampering action of the pleural adhesions. In the right lung many small hæmorrhagic nodules are present, lying close beneath the surface of the lung and confined to the lower lobe. They vary in size between a bean and small nut.

Local condition.—The clitoris is the seat of a soft hæmorrhagic growth, about the size of a Tangerine orange. Along the right side of the urethra, in the position of the bulbous vestibuli, and to a lesser extent on the left, soft friable growth is seen extending forward from a hæmorrhagic mass in the right anterior vaginal wall, measuring $3\frac{1}{2} \times 4$ in. in the vertical and transverse diameter and $2\frac{1}{2}$ in. in thickness. Higher up in the vagina on the left is another large hæmorrhagic mass extending deeply into the cellular tissues between the bladder and the vagina, measuring $4\frac{1}{2} \times 5$ in. \times 3 in. in thickness.

The bladder and urethra were displaced forwards, but are not infiltrated with growth, nor were their functions interfered with during life. In three places the vaginal mucous membrane has given way and hæmorrhagic growth is seen protruding through it. The uterus is enlarged and its muscle soft, but neither the cervix nor the uterine body show any sign of being, or having been, affected with growth, and microscopical section of the muscle fails to show any sign of new growth. The ovaries are small and contain

Primary Embolic Chorion-epithelioma of Vagina.



A. Uterus free from growth. B. Ovaries and Fallopian tubes.
 C. Ureters. D. Cut edges of vaginal wall. E. Vaginal growth.
 F. Urethra. G. Growth involving clitoris.

several small lutein cysts, and the microscopic sections show a fairly large quantity of lutein tissue. These cells are, however, situated mostly in close relation to the cyst walls, and do not appear to disseminate widely into the ovarian stroma proper. Both ureters are lifted up, and can be seen running over the upper limit of the two vaginal masses on their way to the bladder. The growth has not infiltrated above the level of the ureters and the broad ligaments are free from invasion. The inguinal, iliac, and bronchial lymphatic glands contained no growth. At each of the later operations the uterine body was curetted, but the microscopical sections failed to reveal the presence of growth. The sections of all the tumours removed are alike in structure, and are very typical examples of chorion-epithelioma, the syncytium being greatly in excess. The pulmonary nodules are very necrotic and hæmorrhagic, but both varieties of cells can be seen in the sections.

Of course the greatest point of interest in this case lies in the fact that although an intra-uterine vesicular mole was expelled from the uterus this organ remained free from growth, while the vagina became the seat of four separate tumours, which appeared at different times. There was an interval of five months between the removal of the first tumour and the appearance of the second. The chorionic villi must have been lying latent in the perivaginal tissues during this time. When they first appeared each tumour formed a soft but well-defined swelling in the perivaginal tissue, causing little or no local disturbance, but as soon as recurrence and infiltration began the rapid and treacherous manner in which the soft growth spread in the perivaginal tissues was truly alarming. Beyond a slight fulness the infiltration in its early stages caused little superficial alteration either in the skin of the vestibule or the mucous membrane of the vagina, and it was extremely difficult to define the limits of the affected areas until the growth had advanced considerably. I think there can be no doubt that the growth spreads along the perivaginal veins, because the sections taken

from the growing edges show growth creeping along the vessels in the perivaginal tissues, and at the time of the operations small pockets of cells were found in the perivaginal tissues outside the definite limits of the edge of the tumour, while the deeper portion of each tumour had a definite capsule. I should think it was safe to shell such tumours out of their bed when well encapsuled, but the vaginal wall should be removed as widely as possible at the periphery of the growth, in order to avoid the outlying pockets in the perivaginal tissues. The occurrence of these growths in the vagina after the passage of the mole was so symptomless, and the infiltration so insidious, that I think a routine examination should be made for some months after the passage of a mole in every case.

With regard to the diagnosis there is no special difficulty. In the early stages small, soft, perivaginal tumours are liable to be overlooked, and in the later stages the hæmorrhagic infiltrating growth may simulate hæmatoma. The history of a molar pregnancy and the knowledge of the fact that these growths occur will leave no doubt as to the nature of the case.

There are a considerable number of cases now recorded of primary chorion-epithelioma occurring outside the uterus, the uterus having escaped infection.

Two theories have been advanced as to the origin of these tumours: one is that the chorionic villi migrate from the uterus to some more or less remote part, and having settled in the tissues the epithelium of the villi proliferates to form a chorion-epithelioma; the second theory is that the intra-uterine mole is primarily malignant, but the uterus expels it and escapes infection, the growths in other organs being looked upon as metastases. Pick and most authorities are in favour of the first of these theories, and, indeed, it seems improbable that true malignant metastases should form in other organs while the primary growth is expelled from the uterus, leaving that organ free from growth. Again, definite chorionic villi are shown in

the sections of the vaginal growths in many cases. The myxomatous stroma of the villi with its epithelial coverings is easily made out, which seems to suggest that the villus has first migrated and that its epithelium proliferated to form a growth which has the microscopic appearance of chorion-epithelioma. Moreover, it is impossible to determine whether any given specimen of vesicular mole is malignant or innocent when expelled from the uterus, and it is difficult to imagine that a true malignant growth can escape detection when searched for by competent pathologists.

That the uterus may escape is shown in the following cases: Marchand records the case of a patient who died with symptoms of cerebral tumour several months after the removal of a hydatid mole. A large growth was found in the right cerebral hemisphere and small nodules in the lungs and kidneys. The uterus was free from growth, the sections showing decidual remains only. There was no vaginal growth.

A similar case is recorded by Busse, whose patient died four months after an abortion, uterus and vagina also being free from growth.

Among the cases with vaginal growths, those of Lindfors and Schmorl died, and at the autopsy no primary growth was found in the uterine cavity in either case.

In four cases the uterus was removed during life, and on examination no chorion-epithelioma was found. In two cases chorionic villi with some proliferation of epithelium were found in the uterine veins. In the remaining cases curetting and clinical signs were relied upon to prove the absence of a primary intra-uterine growth.

Looking at the microscopical descriptions and drawings of the vaginal growths, we find that typical chorionic villi were found in some parts of the nodule, while sections of other parts showed great proliferation of the epithelium only.

I cannot detect any villous stroma in my sections; the growth seems to consist mainly of masses of proliferating chorion-epithelium. In several of the recorded cases villi were also found to be absent.

I think that the most important question which arises is the degree of malignancy of these primary embolic growths. Even primary uterine chorion-epithelioma, which if not attacked early by operation is, as a rule, so intensely malignant, sometimes behaves in a curiously innocent manner. Noble records and gives drawings of a case in which a great portion of a uterine chorion-epithelioma had to be left behind because it was too extensive for removal. The patient recovered and all signs of the growth disappeared.

Secondary vaginal deposits have disappeared in the same way after hysterectomy for primary uterine growth.

I have collected fourteen certain cases of primary vaginal growths of whom two died. One of them (Schmorl) died eighteen weeks after a normal labour. The second case (Lindfors) died nine months after a normal labour and seven months after removal of the vaginal nodule. In both cases secondary growths were found in the lungs, kidney and liver, but the uterus escaped. The other twelve cases lived, and at the time of reporting were quite well. The nodules were removed in all cases and a full microscopic description is given. In the face of these results one wonders whether these primary vaginal growths are not as a rule almost benign. Judging from two cases recorded by Fleischmann and Eiermann, where the vaginal growth appeared three and a half and four years respectively after the passage of the mole, it seems possible that migrated villi may lie dormant for long periods before proliferation of the epithelium occurs. It is necessary, therefore, to watch these cases for a long time before giving a definite opinion as to the possible occurrence of both primary and secondary growths. That these tumours may be very malignant is shown in the cases of Lindfors and Schmorl and my own.

In the recorded cases of recovery the vaginal tumours were simply excised, and no extensive local operations were undertaken for their removal.

The growths under these circumstances can hardly be

very malignant. This question of malignancy becomes a matter of great clinical importance, not only from the point of view of prognosis but also from that of treatment. If in any given case it can be proved that the vaginal growth is primary the prognosis is probably good, and hysterectomy need not be performed. If, on the other hand, we are dealing with a vaginal nodule secondary to an intra-uterine growth, the prognosis is necessarily bad, and the uterus must be removed at all costs. The microscopical examination of the curettings, together with the clinical signs and symptoms, should give reliable evidence of the presence or absence of an intra-uterine growth.

Apparently the microscopical appearances of the structure of the growth does not help to decide the degree of malignancy. As can be seen in the sections of this case the structure of the growth is that of a typical chorion-epithelioma. Perhaps the arrangement of the two varieties of cells in relation to one another is more regular than that seen in uterine growths, and syncytium is present in larger quantities. In some of the recorded cases typical villi with their stroma are described. Whether the presence of these villi would help to differentiate between primary and secondary vaginal growth is an open question. The vaginal nodules most frequently appear within two or three months after the passage of the mole, but there are four cases recorded in which they made their appearance while the mole was still in the uterus, but, as has been said above, the interval may be as long as four years. The cases which follow full-term pregnancy seem to be more malignant than those following moles or abortion.

With regard to the incidence of lutein tissue overgrowth in connection with primary extra-uterine chorion-epithelioma, it is too early to give a definite opinion either to the frequency or meaning of its occurrence until more control work is done upon the subject of lutein tissue and more notice is taken of the condition of the ovaries in recording cases. In my case the ovaries are not enlarged,

but there is a considerable quantity of lutein tissue present in the sections. The patches of lutein tissue are mostly placed in close relation to the small blood cysts, and there is no diffuse dissemination of lutein cells in the ovarian stroma proper. Schickele, however, describes a case (No. 14 in table) in which both ovaries were enlarged to the size of the fist and contained black lutein cysts. The uterus contained a vesicular mole, simultaneously with a small vaginal nodule, which was removed. Hysterectomy and ovariectomy were performed and the patient was well six months after the operations.

There can be no doubt that trophoblastic cell proliferation is frequently associated with lutein overgrowth, but how the one is directly related to the other must be left an open question until further work has been done upon this most interesting subject.

It seems doubtful whether lutein overgrowth is as often associated with primary extra-uterine chorion-epithelioma as with intra-uterine chorion-epithelioma.

I have seen quite as much lutein tissue in two ovaries not connected with a recent pregnancy as there is in the ovaries in my case.

CONCLUSIONS.

(1) That these vaginal growths most often occur after the passage of a vesicular mole, but, like intra-uterine chorion-epithelioma, may follow abortion or full-term pregnancy.

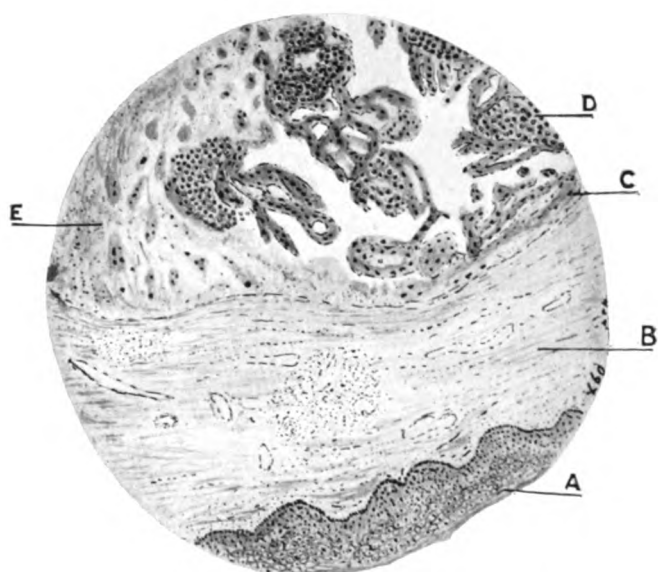
(2) That they may occur while the mole is still within the uterine cavity.

(3) That they originate from the chorion-epithelium of migratory embolic villi.

(4) That there is no evidence to show that a malignant intra-uterine growth or a malignant mole can be expelled from the uterus, leaving that organ free from growth and be followed by metastases in other organs.

(5) That the growth spreads *viâ* the peri-vaginal venous spaces.

Primary Embolic Chorion-epithelioma of Vagina.



A. Vaginal epithelium. B. Vaginal wall. C. Syncytium. D. Langhans' cells. E. Hemorrhage with degenerating syncytial cells.

(6) That there is no means of telling whether any given mole will be followed by chorion-epithelioma.

(7) That the large quantities of syncytium seen in the sections is very characteristic of the vaginal tumours.

I have tabulated shortly the recorded cases found in the literature on this subject.

I have to thank Dr. Taylor for kindly allowing me to make use of this case, and the Clinical Research Association for cutting the excellent sections of the tumours.

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Table of Recorded Cases of Vaginal Chorion-epithelioma.

Author.	Nature of last pregnancy.	Size and position of nodule.	Operation.	Microscopical description of nodule.	Time of occurrence in relation to pregnancy.	Evidence that uterus was free from growth.	Result.
1. Pick (1) (v. Pick and Landau)	Vesicular mole (4 mths.) expelled spontaneously 3 days after expiration of nodule	Nodule size of walnut in anterior vaginal wall	Excision of nodule, curetting of uterus	Mole-vesicles in the coagulated blood, with syncytial proliferation and migrating cells	Simultaneous	Curettings negative	Well 3½ years after operation; two normal pregnancies.
2. Schmorr	Normal pregnancy	Nodule in vagina, metastases in lungs, liver, kidneys, intestines	Post-mortem examination	Typical structure of syncytial tumour	—	Uterus found normal at post-mortem examination	Died 18 weeks post partum.
3. Schlagenhofer	Incomplete abortion	Nodule, size of walnut, immediately behind the commissure of posterior vaginal wall	Excision of nodule. Curetting of uterus	In the coagulum, syncytial masses and Langhans' cells; at the periphery syncytial migrating cells	10 months after abortion	Curettings negative	Well 22 months after operation.
4. v. Guérard	Vesicular mole removed manually	Nodule, size of a big nut on the anterior lip of the os	Vaginal total extirpation of uterus	Enormous broad masses of syncytium	2½ months after evacuation of vesicular mole	Excised uterus free from growth	Quite well 3 years after operation.
5. Schmit (1)	Vesicular mole expelled spontaneously	Tumour the size of a hen's egg on the anterior and left vaginal wall from the urethra to the fornix. Another nodule, the size of a nut, at the posterior point of the columna rugarum	Excision of nodules, curetting of uterus	Large tumour in the coagulum chorionic villi, with layers of Langhans' cells and proliferated syncytium; migrating cells. Small tumour similar, but without villi	3 months after expulsion of vesicular mole	Curettings negative	Well, and menstruating regularly 1½ years after operation.

Author.	Nature of least pregnancy.	Size and position of nodule.	Operation.	Microscopical description of nodule.	Time of occurrence in relation to pregnancy.	Evidence that uterus was free from growth.	Result.
6. Littauer	Vesicular mole (2nd mth.) expelled spontaneously followed by curetting of uterus	Small vaginal nodule	Excision of nodule	Typical chorion-epithelioma	A few months after expulsion of mole	Curettings after expulsion of mole negative	Well 15 months after operation.
7. Lindfors	Normal labour	Walnut-sized tumour at the anterior vaginal wall	Excision of nodule, 8 weeks' post-partum curetting of uterus, and post-mortem examination, large chorion-epithelioma of left lung, smaller nodules in right lung, spleen, brain, and kidneys, and small intestines	In masses of cruro proliferation of syncytium and Langhans' cells. The metastases found post-mortem show all through the structure of typical chorion-epithelioma malignum	First noticed 3 weeks after labour	Curettings negative	Died 7 mos. after excision of nodule.
8. Schmitz(2)	Vesicular mole expelled partially, and remains removed by curetting	Nut-sized nodule on anterior vaginal wall	Excision of nodule, curetting of uterus	In the coeculum chorionic villi, layer of Langhans' cells and syncytium; Typical chorion-epithelioma tissue starting from the surface of the villi; at the periphery syncytial migrating cells	8 weeks after expulsion of vesicular mole	Curettings negative	Well 8 mos. after operation; menstruating regularly.

9. Marchand	Vesicular mole evacuated	No vaginal nodule	Post mortem: tumour in left cerebral hemisphere, nodules in lung and kidney	—	—	Decidual remnants only found post mortem	Died several months after evacuation of vesicular mole.
10. Pick and Landau (2)	Complete abortion	Two pea-sized nodules on anterior vaginal wall	Excision of nodules, curetting of uterus	Within the coagulum are villi with proliferation of Langhans' cells and of the syncytium which are connected with chorion-epitheliomatous tissue; at the periphery migrating cells	2 weeks after abortion	Curetting negative	Well and pregnant 15 months after operation.
11. Neumann	Vesicular mole	Nodule on the anterior vaginal wall	Excision of nodule and hysterectomy	Villi and proliferating epithelium	Simultaneous with mole	Chorionic villus found in uterine vein	Well.
12. Fleischmann	Vesicular mole evacuated	Nodule, size of chestnut, on anterior vaginal wall	Nodule enucleated, uterus curetted	Vacuoles, chromatin nuclei, syncytial cells, no Langhans', no chorionic villi	Nodule appeared 3½ years after evacuation of mole	Necrotic single syncytial cells in the curettings, no attempt at any definite growth formation	Well 1 year after operation.
13. Pöten and Vasmer	Vesicular mole	Small vaginal nodule which recurred 4 weeks later	Excision of nodule, hysterectomy, excised again	Villi and proliferated epithelium	Simultaneous	Chorionic villi in uterine veins	Well some months later.
14. Schickel	Vesicular mole (2 mths.) evacuated	Small nodule on anterior vaginal wall	Nodule excised, hysterectomy and ovariectomy and removal of	Great proliferation of epithelium; distinct villous processes	Simultaneous	Uterus free from growth, but showed	Well 6 mos. after operation.
		2 large lutein cysts from ovaries	cysts from ovaries			necrotic chorion villi in its walls and villi in the uterine veins with some cell proliferation	



(Read before the Clinical Society of London, 1907.)

UPON THE EXTENT TO WHICH WIDAL'S REACTION PERSISTS AFTER RECOVERY FROM TYPHOID FEVER.

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AND

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INTRODUCTION.

It not infrequently happens that hospital patients present themselves with symptoms which suggest the possibility of typhoid fever, and yet give a history of having had typhoid fever, or some febrile attack which was thought to be typhoid fever, previously. The question at once arises whether a positive Widal's reaction in such cases favours the diagnosis of typhoid fever for their present trouble, or whether it may not be due to the former attack. The statements upon this subject in most text-books are very indefinite; sometimes the teaching is "to the effect that the Widal test may remain positive for months and years after the typhoid fever; in other books,¹ that the reaction gradually diminishes in intensity until, after a few years, it disappears entirely.

THE WORK OF OTHERS.

There seem to be few statistics upon the matter. Widal himself¹⁸ repeated his test in seven cases one year after typhoid fever, and found the reaction negative in six, positive in one only. Laming Evans² and Jörgensen³ both worked rather from the point of view of comparing the bactericidal with the agglutinative power of the serum than from that of observing how long it was possible to get a positive Widal's reaction after the fever was past. Evans, using the sedimentation method, repeated the Widal test in twenty-two patients at intervals of two to fourteen months after typhoid fever, and found it positive in five. Jörgensen, on the other hand, found the agglutinative power of the serum diminished very rapidly; it would rise again during a relapse, but when the typhoid fever was over he found the reaction became quite negative in a very few months. He expresses his results in the form of diagrams, Fig. 1 being a typical example.

At the end of this paper will be found references to articles by other observers who have repeated the Widal test in small numbers of patients, but nowhere have we been able to find any statistics covering a considerable number of consecutive cases.

THE SCOPE OF THE PRESENT WORK.

Wishing to find out what was the likelihood of a Widal reaction persisting for months, or years, after typhoid fever, we made a list of all the patients who had given positive reactions when ill with typhoid fever in Guy's Hospital; wrote to each patient; traced as many as we could; sent for these, or went to see them, and repeated the Widal test upon them in the usual way. Our difficulty has been to trace the patients. A great many hospital cases change their addresses frequently, and cannot be followed. Out of 281, we have been fortunate in finding 135 again.

The blood was taken in a Widal tube, and in each case sent to the Bacteriological Laboratory for examination in the routine

*Upon the Extent to which Widal's Reaction persists
after Recovery from Typhoid Fever.*

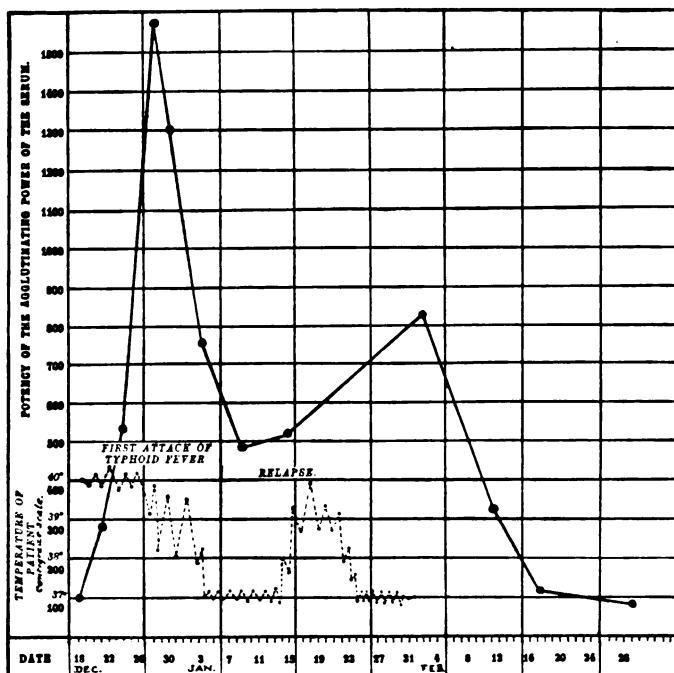


Fig. 1.—Diagram of agglutinative power of blood serum in relation to an attack of typhoid fever and to a relapse.

way. The method adopted was that of the hanging drop, with dilutions of the serum 1 in 20 and 1 in 200, as described in detail by Pakes.¹¹ The examining bacteriologist saw none of the patients, and had no knowledge as to whether the typhoid fever was recent or long past. The results, therefore, are exactly comparable to those that would be obtained in patients who were actually ill. In all cases the cultures of typhoid bacilli clumped readily with the serum of patients suffering from typhoid fever in the wards at the same time, and such patients served as controls throughout the research. Our best thanks are due to Dr. Eyre and Dr. Bainbridge both for carrying out some of the serum tests, and for valuable suggestions as to special points in the work.

THE STANDARD POSITIVE WIDAL'S TEST.

As Pakes¹¹ clearly showed, a positive Widal's reaction should be defined as a complete clumping of the typhoid bacilli within half an hour, when mixed with serum, the dilution being 1 in 200. He showed that out of 326 cases in which the Widal test was tried, 121 proved not to be typhoid fever, and not one of these gave the clumping in half an hour with 1 in 200 dilution of the serum. When less dilution is employed, clumping may be partial or complete, even when the patient has no typhoid fever. With a dilution of 1 in 20, for example, complete clumping within half an hour is not sufficient evidence, by itself, that the patient has typhoid fever; such reaction is suggestive, but it is only partial. In all our cases the Widal's test during the original typhoid fever was complete; that is to say, the patient's serum at that time clumped the typhoid bacilli in a hanging drop preparation within half an hour when the dilution of the serum was 1 in 200. We have kept to the same standard in repeating the test, every specimen being examined in dilutions of both 1 in 20 and 1 in 200, and the results recorded after the preparation had been

standing fifteen minutes and thirty minutes. Expressed as formulæ, the following represent the various degrees of reaction:—

1.—*Negative Reactions.*

Dilution of Serum. Per cent.	Minutes.			Per cent.	Minutes.		
	0.	15.	30.		0.	15.	30.
5	—	—	—	5	—	—	±
0.5	—	—	—	0.5	—	—	—

2.—*Partial Reactions.*

Dilution of Serum. Per cent.	Minutes.			Per cent.	Minutes.			Per cent.	Minutes.			Per cent.	Minutes.		
	0.	15.	30.		0.	15.	30.		0.	15.	30.		0.	15.	30.
5	—	—	+	5	—	±	+	5	—	+	+	5	—	±	+
0.5	—	—	—	0.5	—	—	—	0.5	—	—	—	0.5	—	—	±

3.—*Positive Reactions.*

Dilution of Serum. Per cent.	Minutes.			Per cent.	Minutes.		
	0.	15.	30.		0.	15.	30.
5	—	+	+	5	—	+	+
0.5	—	—	+	0.5	—	+	+

THE RESULTS OBTAINED.

The results obtained are given in a list at the end of the paper, grouped according to the degree of the reaction. The following table gives a summary of the total 135 cases:—

Table summarising the number of cases in each group, irrespective of the time that has elapsed between the original typhoid fever and the repetition of the Widal test :—

	Group A.	Group B.	Group C.	Group D.	Group E.	Group F.	Group G.	Group H.
	Minutes. 0 15 30 5 — — — 0.5 — — —	Minutes. 0 15 30 5 — — ± 0.5 — — —	Minutes. 0 15 30 5 — — + 0.5 — — —	Minutes. 0 15 30 5 — + + 0.5 — — —	Minutes. 0 15 30 5 — ± + 0.5 — — ±	Minutes. 0 15 30 5 — ± + 0.5 — — +	Minutes. 0 15 30 5 — + + 0.5 — ± +	Minutes. 0 15 30 5 — + + 0.5 — + +
Diluted serum, per cent. {								
Total Number in each group: (grand total 135)	81	13	14	10	6	7	3	1
Percentage of the total 135 in each group.	60	10	10	7.5	5	5	2.2	0.3
	Reaction negative. 70 per cent.			Reaction partial, in various degree. 22.5 per cent.			Reaction positive. 7.5 per cent.	

It thus appears that, although in the great majority the reaction becomes entirely negative after recovery from typhoid fever, a positive Widal's reaction may persist in 7·5 cases out of 100, whilst in 22·5 other cases there is a partial persistence of the reaction.

The question at once arises whether the persistence is only for a short time after the fever, or whether it may go on indefinitely. In the following table the cases are arranged according to the time that had elapsed between the typhoid fever and the repetition of the Widal's test:—

Table giving the percentage of negative, partial, and positive Widal reactions at various intervals after the original typhoid fever and positive reaction.

Interval between the original positive Widal's reaction and the time of its repetition.	Negative Reactions.		Partial Reactions.		Positive Reactions.		Total number of Cases.
	No. of Cases.	Per-centage.	No. of Cases.	Per-centage.	No. of Cases.	Per-centage.	
Between—							
1 month & 3 months	2	40	3	60	0	0	5
3 months & 6 months	4	67	2	33	0	0	6
6 months & 1 year	3	100	0	0	0	0	3
1 year & 2 years ...	14	78	4	22	0	0	18
2 years & 3 years ...	13	81	0	0	3	19	16
3 years & 4 years ...	7	100	0	0	0	0	7
4 years & 5 years ...	18	86	2	10	1	4	21
5 years & 6 years ...	12	67	5	28	1	5	18
6 years & 7 years ...	6	40	8	53	1	7	15
7 years & 8 years ...	7	54	2	15	4	31	13
8 years & 9 years ...	4	50	3	38	1	12	8
9 years & 10 years ...	4	80	1	20	0	0	5

It will be seen that time has very little influence upon it. Apparently, if the serum is going to retain its agglutinative power at all, it may do so for many years. In the above table it is obvious that the figures to be dealt with are far too small for any but the broadest conclusions to be drawn from them, but it is clear that the Widal's reaction may in many cases disappear in a very short time, and yet in a few may persist for well over eight years at least. The test has not been in vogue long enough for cases to have been followed up for periods of greater length than this.

Another question which arises is whether the age of the patient at the time of the typhoid fever has any effect upon the persistence of the Widal reaction. In the following table our cases are grouped according to age, and it is quite clear that the Widal reaction is no more likely to persist when the typhoid fever occurs at one age than it is at any other.

Table of cases, grouped according to the age of each patient at the time of the typhoid fever.

Age of patient at the time of the typhoid fever.	Negative Reactions now.		Partial Reactions now.		Positive Reactions now.		Total No. of Cases.
	No. of Cases.	Per-centage.	No. of Cases.	Per-centage.	No. of Cases.	Per-centage.	
5 years old or under	5	72	1	14	1	14	7
Between 5 & 10 years	25	76	6	18	2	6	33
" 10 & 15 years	19	83	3	13	1	4	23
" 15 & 20 years	20	67	8	27	2	6	30
" 20 & 30 years	13	59	6	27	3	14	22
" 30 & 40 years	11	58	6	31	2	11	19
" 40 & 50 years	1	100	0	0	0	0	1

When we investigate the influence of sex, however, we find that females appear much less likely to have a persistent Widal's reaction than are males :—

Table in which the cases are divided according to sex.

	Reaction Negative.		Reaction Partial.		Reaction Positive.		Total number of Cases.
	No.	Per-centage.	No.	Per-centage.	No.	Per-centage.	
Males	59	65	21	23	11	12	91
Females	35	80	9	20	0	0	44

It is true that the total number of cases should be much larger than our 135 to make the point absolutely certain. It is, we think, very unlikely that females never exhibit a persistent serum reaction; but seeing that 11 per cent. of our male, and not one of our female, patients had a persistent positive Widal's test, the above figures are probably more than mere coincidence.

In attempting to find some cause for the persistence of the positive reaction in those cases who had it, we made notes, before the blood was tested, of any prominent complications or sequelæ that were attributed by the patients to their typhoid fever. In the list at the end of the paper these are noted; when no note is made, it implies that the patient had had ordinary enterica without sequelæ. We have picked out the cases in which some suppurative lesion followed the fever, and tabulated them as follows:—

The influence of persistent typhoidal suppuration upon persistence of the positive Widal's reaction.

Widal's Reaction now negative.	{	Case No. 19	Post - typhoidal otorrhœa, still discharging from right ear.	} i.e., out of 94 negative cases, 3 had persistent suppuration = 3 per cent.
		46	Post - typhoidal otorrhœa, quiescent for 8 months.	
		85	Purulent discharge from right nostril ever since typhoid fever.	
Widal's Reaction now partial.	{		No case of persistent suppuration, post-typhoidal.	0.
Widal's Reaction still positive.	{	125	Post - typhoidal empyema, discharging for years.	} i.e., out of 11 positive cases, 3 had persistent suppuration = 27 per cent.
		128	Post - typhoidal otorrhœa, still discharging from both ears.	
		130	Post - typhoidal otorrhœa, still discharging from both ears.	

It will be seen that, although post-typhoidal suppuration, such as otitis media or empyema, seems to render the patient rather more liable to a persistent Widal reaction, the latter may persist without any such cause; and as far as we have been able to judge there is no clinical means of picking out those cases in which the Widal reaction will persist from those in which it will not. This agrees with the views of Jörgensen⁶ and others, namely, that the activity of the serum reaction bears no direct relation to the severity of the disease.

CONCLUSIONS.

Our conclusions are:—

1. That in most cases the Widal's reaction disappears rapidly after the typhoid fever.
2. That in 7·5 per cent. of our cases it remains positive, and may remain so for over eight years, and we do not know how much longer.
3. That the age of the patient at the time of the typhoid fever has little or no influence on the likelihood of this persistence of the Widal's reaction.
4. That the Widal's reaction is apparently more liable to persist in males than it is in females.
5. That the presence of post-typhoidal suppuration somewhat increases the likelihood of this persistence, but is not its only cause.
6. That the cause of the persistence is not known in most cases; and that it is not possible, clinically, to say which patient will, and which will not, give a positive Widal's reaction for years after typhoid fever.
7. That in any given patient, therefore, in whom the present symptoms might be due to typhoid fever, and in whom there is a possibility of a previous attack, the presence of a complete positive Widal's reaction will leave a 7·5 per cent. doubt as to whether this reaction is due to former enterica rather than to the present illness. The great probability is that a complete positive Widal's reaction indicates present typhoid fever.

*Table of cases in which the Widal test with Bacillus Typhosus was repeated months or years after the Widal test was positive during Typhoid Fever.**

GROUP A.†

Cases in which no reaction occurred even in the serum diluted only 1 in 20.

i. e.	Dilution of serum.	Minutes.		
		Per cent.	0	15
	5	—	—	—
	0·5	—	—	—

*The cases were all clinically undoubted cases of typhoid fever. By "positive Widal's test" is understood clumping of the *Bacillus Typhosus* within half an hour when mixed with serum diluted 1 in 200 (Pakes).

† Groups A & B are "negative reactions."

Groups C, D & E are "partial reactions."

Groups F, G & H are "positive reactions."

Case Number.	Sex of patient.	Age of patient at the time of the typhoid fever.	Interval between original positive Widal reaction and the time of repetition of the Widal test.		Special Remarks.
		Years.	Years.	Mths.	
1	M	14	9	9	Had typhoid fever twice; once in 1895, again in 1897. Was in Guy's Hospital with each attack.
2	F	35	9	5	Married.
3	F	9	9	5	
4	M	20	9	2	
5	M	29	8	11	
6	M	20	8	4	
7	M	20	8	1	
8	M	10	8	0	
9	M	10	7	10	
10	F	20	7	6	Married.
11	M	16	7	5	
12	F	18	7	5	
13	F	27	7	2	Single.
14	M	33	6	9	
15	M	35	6	8	
16	M	12	6	7	
17	M	6	6	7	Blepharitis; little or no discharge.
18	M	6	6	3	
19	F	5	6	0	Otitis media after typhoid; right ear still discharges.
20	M	17	5	11	
21	F	39	5	10	Married.
22	M	17	5	10	
23	F	12	5	10	
24	M	5	5	8	
25	M	5	5	7	
26	M	10	5	7	
27	F	32	5	7	Single.
28	M	16	5	4	
29	M	31	5	3	
30	F	11	5	2	
31	M	12	5	0	
32	F	7	4	11	
33	M	19	4	10	
34	M	11	4	10	
35	F	11	4	9	
36	M	9	4	9	Brother of 35.
37	F	26	4	8	Married.
38	F	8	4	8	Has chorea and endocarditis.
39	M	16	4	7	
40	M	19	4	6	
41	F	8	4	5	Just convalescent from severe scarlatina.
42	M	12	4	4	
43	M	7	4	3	
44	F	22	4	3	Married.
45	F	31	4	2	Married.

Case Number.	Sex of patient.	Age of patient at the time of the typhoid fever.	Interval between original positive Widal reaction and the time of repetition of the Widal test.		Special Remarks.
			Years.	Years. Mths.	
46	M	18	4	1	Had had otorrhoea for three and a half years, post-typhoidal. It stopped 8 months ago.
47	M	18	4	1	
48	F	5	4	0	
49	M	12	3	11	
50	M	6	3	11	
51	F	18	3	9	Single at the time of typhoid fever. Married now.
52	F	31	3	8	Married.
53	F	26	3	7	Pregnant 6 months when Widal repeated.
54	F	28	3	3	Single.
55	M	28	3	0	
56	M	41	3	0	
57	M	21	3	0	
58	M	13	3	0	
59	M	7	3	0	Has many glands in neck, ? tuberculous.
60	F	14	3	0	
61	M	10	2	11	
62	M	19	2	7	
63	M	9	2	7	
64	F	25	2	6	Single.
65	M	9	2	3	
66	M	12	1	10	
67	M	10	1	9	
68	M	17	1	8	
69	F	28	1	8	Married.
70	F	27	1	5	Married.
71	F	15	1	4	
72	M	6	1	4	Has double otitis media, but this dates from scarlatina at two.
73	F	21	1	4	Single.
74	M	6	1	3	
75	M	6	1	2	
76	M	9	1	0	
77	M	7	0	7	
78	F	5	0	6	" Chest bad, and going thin."
79	F	10	0	4	
80	F	16	0	2	
81	M	12	0	2	

GROUP B.

Cases in which an indefinite reaction occurred in 30 minutes with serum diluted 1 in 20, but no reaction occurred with serum diluted 1 in 200; nor with 1 in 20 in less than 30 minutes.

i. e.	Dilution of serum.	Minutes.			
		Per cent.	0.	15.	30.
		5	—	—	±
	0.5	—	—	—	

Case Number.	Sex of patient.	Age of patient at the time of the typhoid fever.	Interval between original positive Widal reaction and the time of repetition of the Widal test.		Special remarks.
			Years.	Years. Mths.	
82	M	13	8	1	Has frequent epileptic fits.
83	M	17	7	10	
84	M	12	6	6	
85	M	35	4	5	Has had purulent discharge from right nostril ever since typhoid fever.
86	M	12	2	3	Married.
87	F	32	2	2	
88	M	13	2	0	Brother of 66.
89	M	10	1	11	
90	M	9	1	7	Married. Was pregnant during typhoid. Baby born dead later.
91	F	26	1	2	
92	F	38	0	11	Single.
93	F	17	0	5	
94	M	16	0	4	

GROUP C.

Cases in which a definite reaction occurred in 30 minutes with serum diluted 1 in 20, but no reaction occurred with serum diluted 1 in 200; nor with 1 in 20 in less than 30 minutes.

i. e.	Dilution of serum.	Minutes.			
		Per cent.	0.	15.	30.
		5	—	—	+
	0.5	—	—	—	

Case Number.	Sex of patient.	Age of patient at the time of the typhoid fever.	Interval between original positive Widal reaction and the time of repetition of the Widal test.		Special Remarks.
			Years.	Years. Mths.	
95	M	13	8	4	
96	M	25	8	2	
97	F	20	7	1	Single.
98	F	31	6	10	Married. Is convalescing from influenza.
99	F	24	6	10	Married.
100	M	26	6	9	
101	F	6	6	9	
102	M	8	6	0	
103	F	22	5	9	Married. Is now pregnant
104	M	5	5	4	
105	M	21	5	2	
106	M	19	4	5	
107	F	18	1	1	Single.
108	M	18	0	5	Cough ever since. Looks well.

GROUP D.

Cases in which a definite reaction occurred in 15 minutes with serum diluted 1 in 20, but no reaction occurred with serum diluted 1 in 200.

i. e.	Dilution of serum.	Minutes.			
		Per cent.	0.	15.	30.
		5	—	+	+
	0.5	—	—	—	

Case Number.	Sex of patient.	Age of patient at the time of the typhoid fever.	Interval between original positive Widal reaction and the time of repetition of the Widal test.		Special Remarks.
			Years.	Years. Mths.	
109	M	10	9	3	Has had acne of face and back. Has had bad Malta fever since; also vesical calculus.
110	M	9	8	7	
111	M	16	7	1	
112	M	31	6	10	
113	M	7	6	6	
114	M	17	6	5	
115	M	21	6	5	
116	M	19	5	9	
117	F	13	4	3	
118	M	32	0	1	

GROUP E.

*Cases in which an indefinite reaction occurred with serum diluted
1 in 200, in 30 minutes.*

i. e.	Dilution of serum.	Minutes.			
		Per cent.	0.	15.	30.
		5	—	±	+
		0.5	—	—	±

Case Number.	Sex of patient.	Age of patient at the time of the typhoid fever.	Interval between original positive Widal reaction and the time of repetition of the Widal test.			Special Remarks.
		Years.	Years.	Mths.		
119	M	38	1	6		
120	M	6	1	3		Has a cardiac lesion.
121	F	34	1	2		Rheumatism and dyspepsia ever since.
122	M	13	0	4		
123	F	17	0	3		Single.
124	M	37	0	3		

GROUP F.

Cases in which a definite reaction occurred with serum diluted 1 in 200 in 30 minutes ; but no reaction occurred with 1 in 200 in 15 minutes.

i. e.	Dilution of serum.	Minutes.			
		Per cent.	0.	15.	30.
		5	—	±	+
		0.5	—	—	+

Case Number.	Sex of patient.	Age of patient at the time of the typhoid fever.	Interval between original positive Widal reaction and the time of repetition of the Widal test.		Special Remarks.
			Years.	Years. Mths.	
125	M	34	8	1	Empyema followed typhoid. The sinus discharged till quite recently, though to-day it was healed over.
126	M	8	7	9	
127	M	25	7	8	
128	M	17	7	5	Double otitis media after typhoid, still discharging occasionally.
129	M	28	6	10	Double otitis media after typhoid. Had mastoid operation in London Hospital 9 months ago. Both ears discharge occasionally still.
130	M	11	5	10	
131	M	7	2	7	

GROUP G.

Cases in which a definite reaction occurred with serum diluted 1 in 200 in 30 minutes; and a partial reaction occurred with 1 in 200 in 15 minutes.

Case Number.	Sex of patient.	i. e.	Dilution of serum.	Minutes.				Special Remarks.
				Per cent.	0.	15.	30.	
				5	—	+	+	
				0.5	—	±	+	
Case Number.	Sex of patient.	Age of patient at the time of the typhoid fever.	Interval between original positive Widal reaction and the time of repetition of the Widal test.					Special Remarks.
				Years.	Years.	Mths.		
132	M	21	4	1				Just convalescent from influenza.
133	M	16	2	4				
134	M	33	2	4				

GROUP H.

Case in which a definite reaction occurred with serum diluted 1 in 200, in 15 minutes.

Case Number.	Sex of patient.	i. e.	Dilution of serum.	Minutes.				Special Remarks.
				Per cent.	0.	15.	30.	
				5	—	+	+	
				0.5	—	+	+	
Case Number.	Sex of patient.	Age of patient at the time of the typhoid fever.	Interval between original positive Widal reaction and the time of repetition of the Widal test.					Special Remarks.
				Years.	Years.	Mths.		
135	M	3	7	8				

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THE TREATMENT OF CARIES OF THE RIBS.

By R. P. ROWLANDS, M.S.

TUBERCULOUS disease of the ribs is frequently and mistakenly regarded as trivial, and it is for this reason, perhaps, that such half-measures as "scraping" and "gouging" of the diseased bone have been recommended, and are unfortunately often practised at the present time.

These methods are occasionally successful, but recurrence is all too common, with the formation of sinuses, which may become septic. Re-operation along similar lines usually brings disappointment to the patient and vexation to the surgeon. More radical operations are required for the hopeful treatment of this troublesome condition, which may, if neglected, end in dissemination of the disease.

The two specimens, which have been faithfully drawn to illustrate this brief communication, may serve to show how inadequate any treatment short of resection may be (*vide* Figs. 1 & 2). Both ribs are diseased upon their inner aspects only; the outer surfaces present normal appearances, and do not even suggest the existence of the disease lurking upon the other side.

Figure 1, A & B, represent the outer and inner surfaces of the eighth right rib of a middle-aged man, who had a sinus in the infra-axillary region. Many attempts had been made to cure the condition by opening up the sinus and scraping, but sooner or

later recurrence had always taken place. The sinus had occasionally closed spontaneously, but an abscess had soon formed, and had disabled the patient for a few days, or weeks, as well as lowered his general health.

Before I saw him, the patient had been told that another operation was not advisable, because it was probable that the sinus drained a subdiaphragmatic abscess. Finding no evidence of this, I made a long incision along the eighth rib, exposing it and laying open the sinus, which was traced through the intercostal muscles just above the eighth rib, which it had slightly grooved (*vide* Fig. 1 A). A portion (b c) of the rib was resected, and its inner surface was found to be deeply grooved and carious (Fig. 1 B). It is interesting that the primary resection was not wide enough, because there was so little external indication of the probable extent of any disease. The additional portion (b d) was therefore removed. The caseous wall of an abscess of considerable size was dissected away from the pleura and the diaphragm, the sinus was excised, and the wound was closed. The patient has remained well for a year, and has improved in general health.

The specimen which is represented by Fig. 2, A & B, was taken from a young man who had previously been treated at the Brompton Hospital for "consumption." When I saw him he had few, if any, signs of phthisis, but he had a large cold abscess over the lower and posterior part of the left side of the chest.

The abscess was opened, and its wall, as far as it lay outside the ribs, was dissected out. It was then noticed that a sinus led through the tenth intercostal space into a cavity within the chest. A portion of the tenth rib was excised, under the impression that it was the diseased one, but it was quite healthy. A large abscess cavity was displayed, and found to extend upwards under cover of the ninth rib. On the internal surface of this bone a carious depression was felt, therefore the piece which is figured (Fig. 2, A & B) was resected. It will be noticed that the external surface is smooth and healthy-looking.

The caseating wall of the abscess was carefully dissected away from the pleura and from the diaphragm. A slight recurrence

The Treatment of Caries of the Ribs.

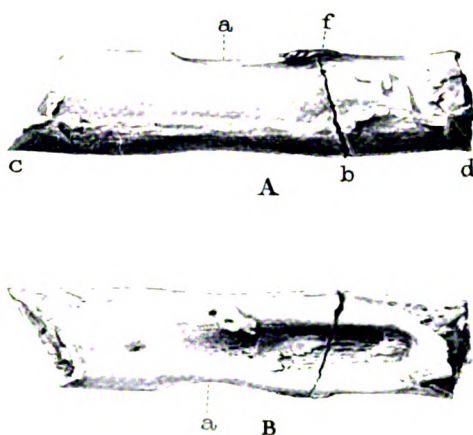


Fig. 1.

Caries of Rib.—A. shows the external surface, and B. the internal surface. A. indicates a slight groove on the upper border. B. shows the disease on the inner surface.

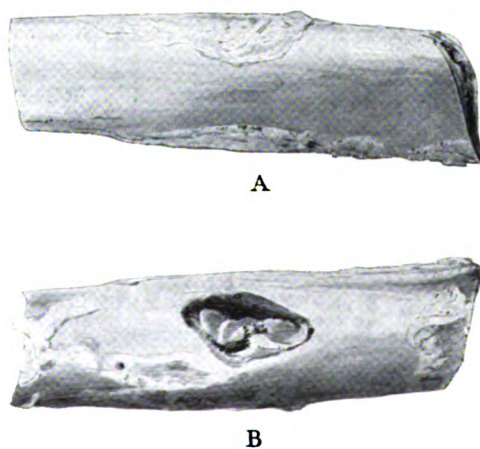


Fig. 2.

Caries of Rib.—A. external surface, apparently quite healthy. B. internal surface, with carious focus.

of tuberculous disease appeared in the scar, but the patient ultimately made a good recovery.

To avoid tuberculous infection of the wound, some surgeons have recommended extirpation of the disease *en masse* without cutting into it, but this can rarely be possible without endangering the pleura, for there is nearly always an abscess on the deeper aspect of the ribs.

Another case may be just mentioned to show the value and importance of resection of a piece of rib as a means of diagnosis and treatment of conditions which may closely resemble caries of the ribs.

A large subpectoral cold abscess was opened through an incision separating the fibres of the pectoral muscle. The wall of the abscess was removed, and a sinus was discovered running into the chest, near the sternal extremity of the third intercostal space on the right side. Therefore, portions of the third and fourth ribs and their cartilages were carefully removed, and a mediastinal abscess was discovered arising from a caseous gland. The abscess was eradicated, and the patient is now well, a year or more after the operation. A scraping operation would have left both the diagnosis and the treatment incomplete.



NEW GROWTHS OF THE TESTICLE.

By G. W. NICHOLSON, M.A., M.D.

(Thesis for the Degree of M.D. Cambridge.)

(From the Pathological Department, Guy's Hospital.)

THE reproductive glands are organs which contain, besides their ordinary epithelium and connective tissue, two special forms of cell which are found in no other organ of the body, namely, the reproductive cells—the ova and the spermatozoa. The function of these cells is to build up a new individual out of their own protoplasm by a process of division. In the higher, and in most of the lower, animals this active growth of the reproductive cells can only take place after the nucleus of the spermatozoon has fused with that of the ovum. In some of the lower animals, however, at all events, the ovum can grow without being “fertilised,” and produce a complete and viable individual. This process is spoken of as parthenogenesis.

We find, when we come to consider the new growths of these glands, that besides those which originate in the epithelium, the carcinomata, and those which originate in the connective tissue, the sarcomata and endotheliomata, there is a third variety. This contains both epithelium and connective tissue. These structures are not found in a simple form, such as we get in a carcinoma or a papilloma, in which there are merely processes of connective tissue with blood vessels, supporting a covering made up of one kind of epithelium. They are found in a highly complicated form, there being skin, glands, teeth,

respiratory and alimentary epithelium, besides bone, cartilage, muscle, and many other tissues. In fact, derivatives of the three primary blastodermic layers of the embryo can be found in them. Now, these tumours, although they occur occasionally in other organs, do so with far greater frequency in the reproductive glands. The inference is therefore obvious, that they are derived from the special cells of these organs—the reproductive cells. These cells, which under normal conditions produce a complete embryo, are able under certain pathological conditions to produce an abortive embryo, in which the normal structure of the body is indicated in a more or less rudimentary and confused manner. These abortive embryos are now called *embryomata*. They have long been known under many names, the most generally-adopted one being, in the case of the testicle, cystic disease; in the ovary, dermoid. These growths often assume a clinically malignant behaviour. This is, no doubt, owing to the young and embryonic nature of the growth, which has got more vitality than the parent in which it originated. An analogous condition is found in normal pregnancy. The mother may be in the last stages of a wasting disease, yet the foetus will be found to be well nourished and healthy.

All the cases described in the present paper, with two exceptions, have been treated, or the specimens preserved, in Guy's Hospital. The two exceptions are cases 60 and 64. The former of these was published by Mr. Strangeways, together with the late Dr. Kanthack. The latter was operated on at Addenbroke's Hospital. I beg to thank the members of the Surgical Staff of Guy's Hospital for permission to make use of the cases; also Mr. Strangeways for allowing me to re-examine and describe his slides of case 60, and Mr. Deighton for permitting me to publish case 64.

It is necessary to add that tumours, such as fibroma, or osteoma, have not been considered, since there was no specimen of such a growth available for examination.

Before treating of the new growths of the testicle, it will be advisable to review a few points in the anatomy and development of this gland, since it is only by the study of the normal structure

of an organ that we can hope to arrive at any knowledge of the diseases to which it is liable.

Sarcoma and carcinoma are very much alike in their histological appearance. Indeed, much confusion exists in the naming of these growths. A definition is therefore necessary of the features which have induced me to place a specimen in the one or the other of these groups.

A sarcoma is a new growth of connective tissue origin, composed of cellular elements resembling embryonic tissue. A matrix of intercellular substance can be traced around each individual cell. This varies both in quantity and quality. The blood vessels show no special tendency to run in the connective tissue, but can often be seen among the cells. In such cases their walls are often composed of sarcoma cells.

A carcinoma is a new growth of epithelial origin. The cells of which it is composed have a considerable amount of protoplasm and a large vesicular nucleus. The structure is nearly always more or less alveolar; the individual cells are not separated by an intercellular substance. The vessels run in the connective tissue of the alveoli. They have a well-marked wall, which is often thickened. The essential cells can often be seen to run in spaces, which in many cases are lymphatics. At the periphery there is usually a fair amount of reaction on the part of the healthy tissues, in the form of a round-celled infiltration.

ANATOMY AND DEVELOPMENT.

Under the tunica vaginalis a few unstriped muscle-fibres belonging to the cremaster internus are inserted into the tunica albuginea at the upper pole of the testicle.

The tunica albuginea is a fibrous envelope, into the deep surface of which the ends of the seminal tubules are inserted into little pits, some of them a few millimetres in length. At the posterior part of the testicle it becomes thickened to form the mediastinum testis, which is perforated by the excretory tubules of the testis, the vasa efferentia. From its deep surface septa radiate into the substance of the gland, dividing it into a number of lobules.

One to four seminal tubules lie in each lobule. These tubules are long (30–175 cm). They give off diverticula which end in bulbed extremities. They communicate with each other and with the tubules of adjacent lobules by numerous anastomoses.

These tubules are embedded in a connective tissue which is fairly loose, and contains, besides the ordinary connective tissue cells, a special form of cell, the *interstitial cells of Leydig*. They are also found in the internal layers of the albuginea, the mediastinum, and the fibrous septa. They are rounded in shape, but may become polygonal from mutual pressure when abundant. Their nucleus is spherical, with several nucleoli and centrosomes. Their protoplasm contains fatty globules, crystals, and pigment granules. They stain readily with eosin. They are said to vary with the activity of the testicle and to be increased in certain forms of new growth. As to their development, some authors maintain that they are of connective tissue origin, whereas others consider them to arise from the epithelium of the tubules.

Around the seminal tubules the stroma becomes condensed, so as to form a special envelope or tunica propria. This consists of three layers :—

a. An external fibro-elastic layer of concentric lamellæ with rod-like nuclei. This appears at puberty.

b. A hyaline layer, very thin in the normal organ, but becoming much thicker in pathological conditions, such as atrophy and new growths. It is non-elastic, and is not in continuity with the outer layer. When thin its staining reactions differ from this layer, but as it becomes thickened, its structure becomes fibrillated and stains like connective tissue. When greatly hypertrophied it becomes convoluted; and finally fills up the lumen of the tubule.

c. A delicate homogeneous membrana propria. On it the seminal epithelium rests directly.

When the seminal canals have reached the last stages of atrophy, the hyaline layer disappears, and nothing is left but the fibro-elastic envelope.

The seminal epithelium is made up of two kinds of cells, the spermatogenic cells and the cells of Sertoli.

The spermatic cells form several layers, and eventually develop into spermatozoa, which for some time before being cast into the lumen of the tubules adhere to the cells of Sertoli. Their nuclei can be seen undergoing mitotic division, and the so-called juxta-nuclear body is seen lying beside the nucleus.

The cells of Sertoli are long and columnar-shaped, with resting nuclei and no juxta-nuclear body. They occur between the groups of spermatic cells and rest on the *membrana propria* by an enlarged extremity, whereas the other extremity projects into the lumen and often has bundles of spermatozoa attached to it. Their function is to nourish the developing spermatozoa.

When atrophy of the tubules occurs, these epithelial cells are seen to undergo fatty degeneration and disintegration, so that nothing is left but a single layer of columnar cells. Later even these cells disappear.

Development.—The sexual gland is developed in the fœtus on the roof of the cœlom, at the angle of junction of the somatopleure and splanchnopleure. The mesothelium lining the cœlom here assumes columnar shape, being called the *germinal epithelium*. Among its columnar cells, at a very early period, some large rounded cells can be seen, the *primordial ova*, which appear not to be formed from it, but to arise at a very early stage of segmentation of the embryo, while it is still a mass of cells or morula. I wish to emphasize this point, since if this is correct, these cells do not arise from any of the three blastodermic layers, but from less differentiated cells, and have, therefore, greater powers of growth and possibilities of development than the more differentiated blastodermic cells, which can only form the various tissues of the primary embryonic layer to which they belong.

As the germinal mesothelium is being formed, the underlying mesoblastic connective tissue becomes condensed. The mesothelium grows down into it in the shape of solid buds, carrying with them the primordial ova. These buds lose their connections with the surface mesothelium, become hollowed out, and form the seminal tubules.

The primordial ova divide, and form eventually the adult ova, or spermatozoa. The columnar mesothelial cells form, in the

testicle, the cells of Sertoli, and in the ovary the epithelial lining to the Graafian follicles.

Duval has, however, propounded the view that the cells of Sertoli arise from incomplete division of the spermatogenic cells, so that the fully-formed spermatozoa are still attached to the basement-membrane. The alternate view is, however, the generally accepted and, I think, the correct one.

The surface germinal mesothelium becomes the visceral layer of the tunica vaginalis.

All the excretory ducts of the testicle are derived from the Wolffian body and duct.

Lymphatics of the testicle.—Within the testicle there are ordinary lymph-capillaries, and also large peritubular channels. These are joined by the lymphatics from the tunica vaginalis and the epididymis. They leave the testicle in the spermatic cord as four to six vessels, which may anastomose, but give off and receive no branches from surrounding tissues. The first gland into which they open is at the level of the lower pole of the kidney. Here there are two to four glands. These communicate with a chain of glands on the aorta on the left side, and between aorta and vena cava on the right. Into the latter, some of the left glands also open.

Behind the large abdominal vessels there is a network of lymphatics and glands which extend downwards to the bifurcation of the aorta and upwards to near the receptaculum chyli. These vessels communicate with those in front of the large abdominal vessels and drain into the receptaculum chyli.

There is an inconstant branch which runs with the vas to the seminal vesicles. This accounts for the rarity with which, in malignant disease of the testicle, the vesiculæ are enlarged.

The fact that the lymphatics, as they run up in the spermatic cord, establish no communication with adjacent parts, explains why metastases in the inguinal glands and in the tissues near the testicle only occur after the growth has penetrated the tunica vaginalis.

CARCINOMA.

In this series of cases there are twenty-five of primary carcinoma of the testicle.

Two forms of this disease have been described, the scirrhus and the encephaloid carcinoma. The former of these is by far the rarer, and there is no example of it in the records of the hospital, although Mr. Bryant published a case in the Transactions of the Pathological Society, xviii., p. 184, which was operated on by him in the hospital. The scirrhus grows slowly, is very hard, and does not attain any great size. It is much less malignant than the encephaloid form.

There are two fairly well-marked varieties of the encephaloid carcinoma, which I propose to call the alveolar and the non-alveolar.

The *alveolar* variety consists of groups of a few (about six to twelve) epithelial cells, surrounded by a scanty amount of connective tissue containing the blood vessels. It bears a strong resemblance to an alveolar sarcoma, for which it is often mistaken, but differs from it in that no connective tissue penetrates between the individual epithelial cells.

The *non-alveolar* variety consists of a more or less open mesh-work of fibrous trabeculæ, in the spaces of which large masses of epithelial cells are packed. These masses may be so large as to occupy several fields under a low power of the microscope.

CASE 1 (Museum No. 2105).—The specimen consists of the half of a testicle, which measures six inches in its longest diameter. The exterior is lobulated, and presents several large irregular bosses, some of which have burst through the tunica vaginalis. The cut surface is entirely composed of masses of a soft, shreddy new growth, separated from each other by fibrous trabeculæ. Many of these lobules are necrotic. Small cysts have been formed by the disappearance of the necrotic tissue. The parietal layer of the tunica vaginalis is firmly and extensively adherent to the tumour. No remains of the testicle are to be seen.

Microscopic appearance.—A carcinoma of the non-alveolar type. The lobules of new growth are separated by thick bands of firm fibrous tissue. There are numerous necrotic areas.

CASE 2 (Museum No. 2107).—Richard S., 40, was admitted in 1858 for a hard, nodulated enlargement of the left testicle, which had been gradually increasing in size for three years. The organ was removed.

Naked-eye appearance.—The testicle measures four inches in length. Its external surface is bossy, and is everywhere covered by the tunica vaginalis. The organ is laid open to show a cut surface which is composed of nodules of whitish new growth, separated by interlacing fibres of connective tissue. No testicular substance can be made out. The epididymis is incorporated with the tumour.

Microscopic appearance.—A carcinoma of the non-alveolar type, which is exceedingly necrotic. There are strands of fibrous tissue with thick-walled blood vessels. No evidence of testicular tubules.

CASE 3 (Museum No. 2108).—Removed from a man of 68, who made a good recovery.

Naked-eye appearance.—Half a testicle, which measures three inches in length, and presents a nodular exterior. The cut surface shows an alveolar arrangement, there being large areas of new growth surrounded by bands of fibrous tissue. The visceral layer of the tunica vaginalis is thickened and infiltrated; the parietal layer is healthy; the testicular substance has disappeared.

Microscopic appearance.—This tumour is so necrotic, and presents such a large amount of leucocytic infiltration, that it is not quite easy to make it out. On examining sections from different parts of the tumour, however, several areas can be found, which show the typical cells of a carcinoma. The new growth is surrounded by a capsule, along the spaces of which it is spreading. Several tubules of the epididymis can be seen, which are surrounded by new growth. This specimen is a non-alveolar carcinoma.

CASE 4 (Museum No. 2109).

Naked-eye appearance.—A testicle twice its normal size. The surface is smooth, and the tunica vaginalis appears to be healthy. The normal epididymis can be seen at the back of the specimen. The organ is laid open to show, in its upper part, an almost round circumscribed tumour. Its smoothness contrasts strongly with the shaggy appearance of the healthy testicle. The new growth is adherent to the tunica vaginalis where it is in contact with it at its upper pole.

Microscopic appearance.—A carcinoma of the non-alveolar type. The masses of new growth are large, and are only separated from each other by a small amount of connective tissue. At the periphery the cells can be seen growing along the lymphatics and connective-tissue spaces in the form of rods of one or two cells in thickness. Here the remains of many testicular tubules are to be found. Their epithelium shows various stages of degeneration from compression, but nowhere does the new growth spread along their lumina.

CASE 5 (Museum No. 2110. Surg. Rep. 1893, Jacobson, 23).—John C., 38, was admitted for an enlargement of the left testicle. He has had a gleet for eight years, which stopped three years ago. Three years ago his left testicle enlarged to the size of a small apple. The scrotum was inflamed, but patient had no pain. He had pinched his scrotum just before. This swelling soon went down, but began to appear again a few months later. It grew steadily until six months ago, when its growth became more rapid. On admission, the left testicle was large, hard, and nodular, with areas of

softening. No distinction [could be made between testis and epididymis. Just above the testicle there was a rounded swelling, the size of a chestnut. It was soft and closely attached to the gland. The cord was slightly thickened. The growth was removed. Patient made a good recovery. After history unknown.

Naked-eye appearance.—The tumour is three inches in diameter and firmly adherent to the tunica vaginalis, the sac of which is obliterated, except at its upper extremity, where it forms a large cyst. Body of testicle and epididymis are uniformly infiltrated with a soft growth with scanty fibrous trabeculae.

Microscopic appearance.—A non-alveolar carcinoma. Very necrotic. At the periphery the alveoli become somewhat smaller. Some very much atrophied testicular substance is visible.

CASE 6 (Museum No. 2113. Insp. 1882, 399. Mahomed. Trans. Path. Soc. xxxiv., 182).—Richard R., 53, was admitted for pain in the lumbar region of six weeks' duration. Three weeks later a swelling appeared in the hypogastric region. On admission there was present a semi-fluctuating tumour, occupying the position of the distended bladder, which rose and fell with the bladder and could not be emptied with a catheter. It was tapped and soft cellular material withdrawn. There was swelling of the left leg, and dulness at both bases. Death occurred suddenly.

Post-mortem inspection.—Body wasted. No ascites or oedema of legs. Deposits of new growth were found in the muscles of the back, thymus, cervical glands, both pleura, a bronchial gland which had completely obstructed the bronchus to the middle lobe of the left lung and oesophagus. A large mass of retro-peritoneal glands, in which both kidneys, the pancreas, suprarenals and duodenum were embedded, and which compressed the bile ducts. The growth had fungated into the lumen of the duodenum. The kidneys were cystic, and the bile ducts in the liver were distended, so that this organ looked cystic. The gall-bladder was full. No jaundice. No growth in lungs, liver, or kidneys.

The right testis was undescended. It weighed thirty-six ounces and occupied the position of the distended bladder. It retained its shape. The epididymis was normal. The growth was completely non-adherent, the peritoneum not being involved. It was attached by a pedicle formed by the vas and spermatic vessels. The internal abdominal ring was closed. The left testicle was normal. On section the gland was uniformly infiltrated with a shreddy and necrotic new growth.

Microscopic examination.—This tumour, which is very necrotic, is a carcinoma of the alveolar type.

CASE 7 (Museum No. 2116).—George J., 40, had noticed his testicle to be enlarging for five years before removal by Sir Astley Cooper in 1807. The enlargement was attributed to injury.

Naked-eye appearance.—The tumour is four inches in length. It is uniformly enlarged and occupied by a homogeneous growth with a smooth surface and a few trabeculae. The two layers of the tunica vaginalis are partially adherent.

Microscopic appearance.—A non-alveolar carcinoma. The growth can be seen spreading down the lymphatics. No testicular substance visible.

CASE 8 (Museum No. 2117).—From a man of 48, whose testicle was removed in 1864, and who made a good recovery.

Naked-eye appearance.—The testicle is four inches in length, and is uniformly infiltrated with a white growth with fibrous trabeculae. The upper part is shreddy from degeneration. The tunica vaginalis is adherent.

Microscopic appearance.—A carcinoma of the non-alveolar type. Except at its spreading edge it is completely necrotic. Some of the masses of non-staining necrotic cells are infiltrated with well-staining leucocytes. They are invaded by granulation tissue, which eventually replaces them.

CASE 9 (Museum No. 2120).—This specimen was removed from a man of 30, who had noticed a gradual enlargement of the right testicle for nine months. His health was good a year after removal.

Naked-eye appearance.—An injected testicle, uniformly enlarged, so as to measure three and a-half inches in its longest diameter. The exterior is smooth, and the tunica vaginalis normal. The cut surface shows the gland to be infiltrated with a soft necrotic growth with ragged cavities. A thin layer of testicular substance is spread out over the upper part of the tumour. The epididymis does not appear to be involved. The globus major is flattened out over the upper, and the globus minor over the lower pole of the tumour.

Microscopic appearance.—A non-alveolar carcinoma, which is exceedingly necrotic. Some very much atrophied testicular substance and healthy epididymis can be seen.

CASE 10 (Museum No. 2124).

Naked-eye appearance.—A testicle, somewhat enlarged. The exterior is smooth, and the tunica vaginalis is not invaded. The cut surface shows a soft new growth, which is divided into lobules by trabeculae of white fibrous tissue. No testicular substance is visible. The epididymis appears to be normal.

Microscopic appearance.—A carcinoma of the alveolar type. It can be seen spreading between the testicular tubules, which become atrophied, and are finally represented by solid hyaline rods. Some of the tubules become invaded by the new growth which bursts through their capsules.

CASE 11 (Museum No. 2125. Surg. Rep. clxxiii., 169).—Robert F., 26, was admitted for an enlargement of the right testicle. He is married and has two children. Fourteen or fifteen years ago he pinched the testicle, which gave him pain for some time. There was no trouble until seven months ago, when the gland suddenly enlarged and became very tender. He has had frequent pinches from the saddle when riding. When he first noticed the tumour it was of its present size. On admission, the right testicle was three times its normal size, and there was a hard nodular swelling at the situation of the epididymis, which was tender. The growth was removed. Recovery good. After-history unknown.

Naked-eye appearance.—The testicle measures three inches in length. The surface is bossy, and is covered by the thickened visceral layer of the tunica vaginalis. The cut surface presents closely aggregated nodules varying in size from half a line to nearly an inch in diameter. The nodules are soft and have undergone less contraction from the action of the preserving

fluid than has the stroma. They thus form rounded elevations. The testicular substance has disappeared. The epididymis appears to be healthy.

Microscopic appearance.—A carcinoma of the alveolar type. There is a good deal of round-celled infiltration in the fibrous trabeculae at the periphery of the nodules.

CASE 12 (Museum No. 2126).—Presented by Sir Astley Cooper. This tumour is three inches in length, and is composed of a uniform new growth with a few trabeculae. The exterior is smooth and does not adhere to the tunica vaginalis. The epididymis is normal.

Microscopically.—A carcinoma of the alveolar type. The alveoli, however, are larger than usual. No testicular substance visible.

CASE 13 (Museum No. 2127. Surg. Rep. cxxiv., 2).—William R., 48, was admitted in April, 1886, for a tumour of the left testicle. In October, 1884, he was struck by a piece of wood in the scrotum, and experienced severe pain for a few minutes. In May, 1885, he noticed the testicle to be enlarged. It was painful and tender. In December it began to swell again, after a running match. He stated that it had always been larger than the right testicle. On admission, the left testis was large, hard, and nodular. No pain or discomfort. It had doubled in size during the last three months. The tumour was removed, and a large hydrocele was found. Patient was readmitted in November, 1886, with a recurrence in the scrotum, which was fungating. It was removed, and found to spring from the stump of the cord. It shelled out easily. On being cut into, a cavity with granulations was seen. In March, 1887, he returned with an enormous recurrence in the left inguinal and lumbar glands, and cedema of the left leg. After-history unknown, but cannot have been long.

Macroscopic appearance.—A part of the tumour, whose weight was twelve ounces. Growth soft and white, with a few trabeculae. Lower part necrotic. Tunica vaginalis adherent.

Microscopic appearance.—A carcinoma of the alveolar type. The lobulation is very distinct.

CASE 14 (Museum No. 2128. Green Insp., v. p. 150).—Jonathan K., 28, was admitted in 1828 for a swelling of the right testicle, which had been noticed for five years. There was no pain. Fluctuation could be obtained. Patient had an attack of scarlet fever after admission. The tumour was punctured and blood drawn off. The scrotum then became gangrenous. Sir Astley Cooper considered the tumour to be merely chronic, and such as might be removed by a long-continued course of salivation. Nevertheless, patient died on the seventh day after admission. The tumour measures four and a half inches in length and presents numerous areas of softening. The tunica vaginalis is adherent everywhere, except at its upper part, where it is coated with puriform lymph.

Histology.—A carcinoma of the alveolar variety, which can be seen to spread down the lymphatics. No testicular tubules visible. It is very necrotic in places.

CASE 15 (Museum No. 2129).—Thomas J., 56, was admitted under Mr. Hilton in 1855 for a swelling of the right testis, [which had been gradually increasing for twelve months.

Naked-eye appearance.—The tumour is four inches in length, and is made up of a soft growth with a few trabeculae. The surface is irregular, and the tunica vaginalis adherent.

Microscopic appearance.—An alveolar carcinoma, which is very necrotic.

CASE 16 (Museum No. 98⁹⁶. Surg. Reg., No. 115. Surg. Rep. 1898, Golding-Bird, 299).—Henry B., 38, was admitted on May 14th, 1898, for a tumour of the left testicle. Since boyhood this testicle has been bigger than the other, but both were of the same consistency. Eighteen years ago he had an attack of orchitis for a few days after an injury. Three years ago it began to grow gradually and has caused him some little pain. On admission, the testicle was hard and painful in its upper part. The scrotal veins on the left side were distended and the cord was thickened. May 17th, castration. Patient left the hospital on June 1st, with the wound still open, contrary to advice. After-history unknown.

Naked-eye appearance.—The tumour measures six inches by four. On section it is grey, soft, and friable. The tunica vaginalis is thickened and coated with old blood clot, and is being invaded by the new growth. The testicular substance is unrecognisable.

Microscopical examination.—This growth consists of fairly firm fibrous trabeculae set widely apart, and containing some thickened blood vessels. Its meshes are filled with a mass of closely-packed cells, between which no connective tissue can be traced. Small pieces of fibrous tissue, some of which contain a blood vessel, can be seen here and there. They are obviously trabeculae cut across. Extensive areas of necrosis occur. This growth is a carcinoma of the non-alveolar type.

CASE 17 (Surg. Reg. No. 804. Surg. Rep., 1900, Howse, 389).—W. F. H., 41, was admitted for enlargement of the right testicle, which he had noticed for eighteen months, when it was the size of a pigeon's egg. He had lost two stone in weight during the last two years. On admission, patient was thin and wasted. The right testicle measured thirteen and a-half inches in circumference, seven inches in length. It was pear-shaped, hard, and smooth, with one elastic spot. The scrotal veins were distended. The cord was thickened and the lumbar glands could not be felt to be enlarged. The liver extended to within an inch of the umbilicus. A large hard mass could be felt in the lumbar region. The lungs were normal. The testis was removed. Recovery was uneventful. Nothing is known about the after-history of this case.

Macroscopically the tumour consisted of masses of breaking-down tissue surrounded by hard fibrous material. It contained a few cysts filled with thick brown fluid.

Microscopically.—A medullary carcinoma of the non-alveolar type with wide fibrous trabeculae. Connective tissue cannot be traced between the cells. There are thickened vessels in the trabeculae.

CASE 18 (Surg. Reg. No. 1028. Surg. Rep. 1901, Golding-Bird, 296).—George William P., 31, was admitted for an enlargement of the right testicle. He is married and has one child. A year ago the right testicle enlarged and was painful, but soon recovered under treatment. No injury is mentioned. The enlargement recurred a month later, and has steadily increased. On admission the right testicle was large and pyriform. It was hard and tender. Fluctuation could be obtained. The testicle was removed. After history unknown.

Macroscopically.—It is stated that the new growth surrounded the remains of the testicle.

Microscopically.—At first sight this specimen resembles a sarcoma, there being an appearance of connective tissue between the cells. This appearance is due to a degeneration of the cell protoplasm, which is granular at its periphery, and thus produces it. In one part, in which the cells have disappeared, there remains a network of fibrous trabeculae, the spaces of which correspond in size to the alveoli of the growth. No connective tissue is to be seen within these spaces. The blood vessels in many places are thick. We are, therefore, dealing with a carcinoma of the alveolar type. Degenerated seminal tubules are visible, whose epithelium has disappeared, and which are represented by solid hyaline rods.

CASE 19 (Surg. Reg. No. 1109. Surg. Rep., 1901, Golding-Bird, 516).—Joseph J., 59, was admitted for a painless enlargement of the right testicle, which had been noticed for six months, during which time it steadily increased in size. On admission the right testicle measured five and three-quarter inches in length and twelve inches in circumference. It was firm above and soft below. The tumour was removed. I received a postcard in November, 1906, from patient, to say that since the operation he has been fairly well.

Microscopically.—A carcinoma of the non-alveolar type. It is very necrotic. The new growth can be seen extending down the lymphatics.

CASE 20 (Surg. Reg. No. 1244. Surg. Rep., 1902, Lane, 40).—Robert J., 38, was admitted for an enlargement of the left testicle, which had been growing steadily for a year. There is no history of injury. Sometimes he experienced slight pain in the morning. Patient is married and has two children. On admission, the tumour was hard, with an area of softening. The prostate was enlarged. The organ was removed. The epididymis and vas were found to be normal. In November, 1906, patient writes to say that he has been in good health ever since leaving the hospital.

Microscopically.—A carcinoma of the non-alveolar type. There are some seminal tubules, apparently unaltered, to be seen.

CASE 21 (Surg. Reg. No. 1270. Surg. Rep. 1902, Steward 23).—Samuel D., 61, was admitted for a tumour of the right testicle. He is the father of nine children. Ten months ago he noticed a hard and painless swelling of the size of a walnut, which has grown ever since. On admission, the right testis measured four inches in diameter. It was hard, heavy, globular, and somewhat elastic, with lowly-rising bosses. Slightly flattened

at sides. There was no pain or tenderness. A small area at the upper part of the tumour was translucent. It was removed. After-history unknown.

Microscopic examination.—A carcinoma with very distinct alveolation. The cells are large and closely packed, and the vessels run in the stroma.

CASE 22 (Surg. Reg. No. 1618. Surg. Rep. 1903, Dunn, 116).—Arthur H., 47, was admitted for a tumour of the left testicle, which he had noticed for two and a half years. It had been growing steadily, and attained its present size four months ago. Eighteen months ago growth became more rapid. He is married and has twelve children. Testicular sensation was said to have been lost for a year on both sides. On admission, the left testicle was thirteen inches in circumference. It was softer above than below, and caused no pain, except after being handled. There was a small hard mass at the posterior part of the tumour, which had only been noticed for a week. The cord was thickened and the inguinal glands were palpable. The growth was removed. Patient alive and well in November, 1906.

Microscopic examination.—A carcinoma of the non-alveolar type. The epithelial cells are large, with large nuclei. The connective tissue trabeculae are very wide apart and contain the blood vessels.

CASE 23 (Surg. Reg. No. 2437. Surg. Rep. 1905, Symonds, 561).—Henry William H., 35, was admitted in September, 1905, for an enlargement of the right testicle, which was first noticed in July or August, 1903. He is the father of one child. The growth did not increase uniformly, but would remain stationary for two or three weeks and then grow larger in a few hours. There was no pain until ten days before admission. No history of injury. Patient has lost weight. On admission, the right testicle was large, oval, and trilobulated. There was no pain, but some discomfort. The cord was not thickened. Castration was performed. Recovery uneventful. In November, 1906, patient wrote to say that since leaving the hospital his health has been good. He has been able to follow his employment, which necessitates a good deal of walking, without a break. He has put on weight.

Histological examination.—A carcinoma of the alveolar type. There are delicate connective tissue trabeculae enclosing alveoli that are closely packed with epithelial cells, up to twenty or more in each alveolus. The blood vessels which run in the larger trabeculae are thickened. Many lymphatic vessels filled with new growth can be seen. Numerous seminiferous tubules are scattered about which are filled with cells. In some of these the cells can be seen piercing and destroying the tunica propria; nowhere does this membrane show any appreciable thickening.

CASE 24 (Surg. Reg. No. 2779. Surg. Rep., 1906, Lane 384).—John D., 50, was admitted in July, 1906, for an enlargement of the left testicle. He is married and has seven children. Eighteen months ago he had a fall, which put a severe strain on his lumbar region. The same day he noticed the testicle to be the size of a hen's egg. It was painful for a few days only. This swelling has gradually increased in size. On admission, the left testicle was twelve inches in circumference, longitudinally, and six inches transversely. Fluctuations could be obtained, and the anterior part of the swelling was

translucent. The cord was not thickened. There was no evidence of metastasis. The testicle was removed and a small hydrocele found.

Naked-eye appearance.—The tumour still presented the shape of the testicle. It was smooth, except for a few lowly-rising bosses. The tunica vaginalis was not pierced by the growth, and its two layers were not adherent. The growth was very vascular. The epididymis was stretched out behind the tumour.

Microscopic appearance.—A carcinoma of the alveolar type, the alveoli being very large in places. At one spot the new growth is seen invading the albuginea. The blood vessels, which run in the trabeculæ, have distinct walls. No seminal tubules can be seen.

CASE 25 (Surg. Reg. No. 2853. Surg. Rep., 1906, Fagge, 148).—Ernest D., 37, was admitted in November, 1906, for an enlargement of the right testicle. It is said, five years ago, to have suddenly enlarged during the night. It was relieved with suspension and iodine. Twelve months later a similar attack occurred. Since December, 1905, the organ has steadily increased in size. On admission the testicle was the size of a goose's egg. There was no pain. A slightly enlarged gland was found in the right groin. Patient is a healthy, strong-looking man. Castration was performed, and a small hydrocele found.

Macroscopic appearance.—The tunica vaginalis is adherent, except above, where a space occupied by the hydrocele can be seen. The epididymis cannot be made out. The surface of the growth presents various bosses, but the growth has not fungated through the tunica vaginalis. The cut surface presents a shreddy grey appearance, with large necrotic areas. Below, there is a firmer white area.

Microscopic appearance.—A carcinoma of the alveolar type with large areas of necrosis. There is a marked amount of leucocytic infiltration, which, beginning in the connective tissue trabeculæ, has in many places entirely replaced the cancer cells. The blood vessels are remarkably thickened. My sections show no remains of testicular tubules.

CONCLUSIONS.

In this series of twenty-five cases of primary carcinoma of the testicle, the only form of cancer which occurs is the spheroidal-celled. This may be either a scirrhus, of which there is no example, or a soft, encephaloid cancer. The latter I have sub-divided into two forms: (a) The alveolar form, in which the connective tissue forms a delicate, small-meshed network, in the interspaces of which only a limited number of cells are closely packed together. It differs from an alveolar sarcoma, for which indeed it is generally mistaken, in that no connective tissue can be traced between the epithelial cells, which have large, rounded nuclei with distinct nucleoli. The cells of the

connective tissue retain their elongated form and small nuclei. No transitional stages are to be seen between them and the malignant cells. There often is a large amount of leucocytic infiltration in the connective tissue trabeculæ, so that the alveoli of malignant cells appear to be separated from each other by thin bands of leucocytes. (*b*) The non-alveolar form, which resembles any medullary spheroidal-celled carcinoma. Here the connective tissue is arranged in large, more or less coarse and thick trabeculæ, including spaces which are often so large as to be visible with the naked eye. These spaces are closely packed with the epithelial cells without the intervention of any connective tissue. I presume that a scirrhus of the testicle would conform to this type, the fibrous trabeculæ being merely thickened and in excess of the malignant cells. In both these sub-groups the blood vessels run in the connective tissue, and do not penetrate between the epithelial cells. This explains the common occurrence of necrosis in the centres of the masses of cells in the non-alveolar variety: the central cells are unable to gain sufficient nourishment, and therefore die. In the alveolar type the alveoli are so small that all the cells can receive an adequate amount of food. Necrosis is, therefore, much less common in this form.

As regards the relative frequency of these two forms, the alveolar occurred twelve times and the non-alveolar thirteen times.

Origin.—There can be no doubt that carcinoma originates in the epithelium of the seminal tubules. This fact was first pointed out by Birch-Hirschfeld in 1868. The cells of the new growth closely resemble those of the seminal tubules. Indeed, it is often difficult at first sight, on examining the tubules at the periphery of a tumour, to arrive at a decision as to their being ordinary epithelium or new growth. A difficulty now arises. According to most authorities on embryology, the germinal epithelium is derived from the mesoblast, and the growth is therefore not, strictly speaking, a carcinoma at all, but a sarcoma. But the whole appearance and characteristics of these tumours necessitate the belief in their carcinomatous nature. They

present all the features of carcinoma and none of sarcoma. There can be no doubt, however, that the last word has not yet been spoken on the development of the reproductive glands. Nobody calls the ovarian epithelial growths sarcomata, and we must assume a similar origin for them. Two explanations may be offered. One is, as suggested by Foulerton, that the Wolffian elements penetrate farther into the testicle than is generally supposed, and that the seminal tubules are epithelial and not mesothelial. The growths are, then, carcinoma and not sarcoma. Another explanation can, I think, be found in the assumption that the spermatogenic cells have been derived from the primordial ova, which have been separated off from the blastomere at a very early stage of development, and have wandered into the reproductive glands. There, as I shall point out when dealing with the embryomata, they may, under pathological conditions, produce an embryoma. On the other hand, they may differentiate into the normal epithelium of the seminal tubules, and eventually form spermatozoa. Now, a pathological condition may set in, the cells do not fully differentiate into spermatozoa, but proliferate and produce a carcinoma. If we assume, therefore, that the pr  mordial ova are undifferentiated cells, there is no reason why their descendants, in differentiating, should not assume an epithelial type and give rise to an epithelial new growth—true carcinoma.

Naked-eye appearance.—These tumours form large, rapidly-growing smooth swellings, which for a long time retain, more or less closely, the shape of the testicle. They eventually make their way through the tunica albuginea, and there give rise to the appearance of lowly rising bosses on the surface of the tumour. The tunica vaginalis is not invaded until very late. It is usually thickened from inflammatory reaction, and the two layers often become adherent from the same cause, with the production, in some cases, of an hydrocele. This late bursting of the growth through its coverings is well shown in case 6, where the testicle was retained in the abdomen. Although it weighed thirty-six ounces it retained its normal shape, and there was no sign of invasion of the peritoneum.

The cut surface presents a homogeneous, soft, brain-like appearance, with a few connective tissue trabeculæ, occasional hæmorrhages and shreddy cyst-like cavities produced by extravasated blood and disintegration of the tissues.

History.—Only a few points need be mentioned.

The average age of the patients at the time of the operation is forty-three. The youngest is twenty-six and the oldest sixty-eight. Fourteen cases occurred between the ages of thirty and fifty.

The average duration of the disease before operation is one and a half years, the maximum being five years and the minimum six weeks. These figures, of course, are not very reliable, as the patient probably did not notice anything wrong until the tumour had appreciably increased in size. Case 16 had his testicle enlarged from boyhood; it began to grow actively three years before admission. It is quite possible that it may have been an embryoma, which began to undergo a malignant change three years ago, and when removed had been entirely obscured by the carcinomatous change (cf. Embryoma, case 2). This possibility cannot be excluded in some of the other cases.

There is a very marked history of injury, or prolonged irritation, such as a gleet or repeated attacks of orchitis.

The subsequent duration of life it is hard to be certain of, since so many patients have been lost sight of. Among nine cases whose after-history could be traced, one is alive 5, one 4, one 3 years, one 1 year, and two some months after the operation. Two died in hospital within a short time of the operation, and one was seen in a moribund condition after eighteen months. The outlook, therefore, is bad. Taking three years to mean comparative safety, only three out of ten patients can be said to be cured.

I shall discuss what I have to say about metastasis after dealing with sarcoma.

Columnar-celled carcinoma.—In this place it need only be mentioned that a columnar-celled carcinoma of the testicle does not occur in this series of cases. Many instances were described some years ago; but on reading the descriptions of

them, it is obvious that they were embryomata. Butlin, in 1882, quite rightly pointed out that the only variety of cancer hitherto observed is the spheroidal-celled. Foulerton has recently described a case of columnar-celled carcinoma, but from his description and figures, it is evident that he was dealing with an embryoma.

SARCOMA.

CASE 26 (Museum No. 2112. Insp. 1862, 1).—Samuel S., 15, was admitted for paralysis of both legs and anæsthesia as high as knees, which had commenced five weeks before with pains in the back. The paralysis spread upwards until respiration became affected. Arms remained free. A tumour was felt in the lower part of the abdomen.

Post-mortem inspection.—Body spare. Slight bed sore. A large mass was found in the upper dorsal region, infiltrating the muscles of the back, penetrating between the vertebral arches and attached to the dura mater. The cord was extensively softened between the cervical and lumbar enlargements, which appeared healthy. Growing from the left part of the foramen ovale there was a cancerous tumour, about the size of a small walnut, which projected into the right auricle. A large mass in the wall of the lower end of the jejunum, with some enlarged glands. Several large masses of growth in the kidneys. Both epididymes and the left vas contained new growth. Testes free.

Naked-eye appearance.—Both epididymes are enlarged by a uniform white growth. There is a deposit in the left spermatic cord. The testes appear quite healthy.

Microscopic appearance.—Small round-celled sarcoma, showing the remains of the tubes of the epididymis.

CASE 27 (Museum No. 2114. Surg. Rep., vol. cxxxii., 13a. Insp. 1888, 197).—John C., 72, had a large tumour in the right side of the scrotum ever since he could remember, and a hernia for forty years, for which he had worn a truss. He is the father of eleven children. Three months ago a swelling appeared in the right groin, which has gradually become larger and harder. There is a good deal of pain on the inner side of the thigh.

On admission.—A large tense tumour in the right side of the scrotum, extending to just below the abdominal ring; six and a half inches in length and thirteen in circumference. Another hard lobulated tumour in the right groin. Fixed to deep tissues; no enlarged iliac or lumbar glands could be made out.

Post-mortem inspection.—Extreme dropsy of both legs. Fluid in both pleura. No deposits in lungs. A large growth in right inguinal region and half of pelvis, pushing up peritoneum. Adherent to skin and capsule of hip, blocking external iliac vein and compressing artery, invading bladder. Liver, kidneys, and lumbar glands normal.

Naked-eye appearance.—The whole tumour is converted into a large cyst by a process of degeneration. Its wall is formed by the tunica albuginea. The cavity measures six inches by three and a half, and was filled, in the

recent state, with fourteen ounces of brown mucoid fluid. At the lower and anterior part are seen shreddy remains of the original growth. The tunica vaginalis is obliterated at its lower part. Cord normal, except where it pierced the inguinal tumour.

Microscopic appearance.—A small round-celled sarcoma.

CASE 28 (Museum No. 2118).—Richard E., 25, was admitted in 1860 for an enlargement of the right testicle, which had been noticed for three years. Three months previously the tumour was punctured, after which proceeding it rapidly increased in size, and on admission was found to be pulsating. It was removed. Patient recovered.

Naked-eye appearance.—The tumour is six inches in length and shows below a homogenous growth with some fibrous trabeculae. At the upper part the growth is softer, and presents many large ragged cavities, some of which contain blood clot. The exterior is smooth. The tunica vaginalis is thickened, but its layers are not adherent to each other.

Microscopic appearance.—A small round-celled sarcoma.

CASE 29 (Museum No. 2130).—Removed from a child of six, whose mother had noticed a rapidly increasing swelling for five months before removal.

Naked-eye appearance.—The tumour is two and a-half inches in length, and infiltrated with a white gelatinous growth. The surface is nodular.

Microscopic appearance.—The matrix of this tumour is exceedingly oedematous, so that it may be aptly called a myxo-sarcoma. The cells are small; they are mostly round, but a fair number of spindle and stellate cells are to be seen. Every here and there one finds a large cell with one or more nuclei. The new growth is separated from the remains of the testicle by a thick fibrous capsule, which, however, it is invading. The testicle is of the infantile type. Some of the seminal tubules show signs of atrophy. The epididymis is healthy.

CASE 30 (Surg. Reg. No. 470. Surg. Rep., 1899, Howse, 361).—Thomas N., 52, was admitted in July, 1899, for an enlargement of the right testicle. He is married, and has healthy children. In November, 1897, he fell and squeezed the testicle violently. There was great pain, which soon disappeared with rest. Two or three weeks later he noticed a small nodule in the testicle, which swelled to the size of a fist. In January, 1898, a large blood-clot was removed, which relieved him. The swelling, though painful, increased slowly and steadily. A week ago two clots appeared through a small sinus in the middle of the scrotum. On admission, the right testis was large, hard, and inflamed. There was a small median sinus, exuding watery, blood-stained discharge. The mass was hardest above, softer below. The cord was thickened. The lumbar glands were not enlarged. Castration. Primary union. After-history unknown.

Microscopically.—A small round-celled sarcoma, which is very necrotic.

CASE 31 (Surg. Reg. No. 1063. Surg. Rep., 1901, Lucas, 340).—Frederick H., 36, was admitted for an enlargement of the right testicle. Five months ago he had a dull aching pain in it, but did not notice any swelling until two months later. It decreased slightly with suspension. He complains of occasional severe shooting pains, radiating to the right inguinal region. On

admission, the right testicle measured seven and a half by three inches. It was kidney-shaped, flattened antero-posteriorly, tense, and smooth. Translucent above. The cord was thickened. Above the external abdominal ring there was a small, hard, moveable, tender mass, which had been noticed for three weeks. The iliac glands were felt to be enlarged. There was also a small tumour above the umbilicus. The right vesicula seminalis was thickened. The tumour was removed. Recovery uneventful. After-history unknown.

Naked-eye appearance.—The upper pole of the testis contained soft gelatinous breaking-down material, with necrotic areas.

Microscopic appearance.—A small round-celled sarcoma.

CASE 32 (Surg. Reg. No. 1484. Surg. Rep., 1903, Dunn, 28).—Ernest R., 35, was admitted in February, 1903, for an enlargement of the left testicle, which had been noticed for six months. A month ago a small painful swelling appeared in the left parotid region. It was hard at first, but has softened lately. Five days ago his left hip became very painful. His left iliac region is tender. On admission, the left side of the scrotum was occupied by a mass which extended to the external abdominal ring, was pear-shaped and hard. Painless. Skin moveable over it. There were enlarged glands in both groins, bigger in the left. The swelling in the left parotid was fixed to the deep structures, but not to the skin, which was normal. An area of anæsthesia was made out just below the left angle of the mouth. The testicle was removed. Some organising clot was turned out of the scrotum. A small nodule was found in the cord. The parotid was punctured and a small amount of pulpy material mixed with blood withdrawn. Patient was discharged on March 3rd with primary union, but an increase of the parotid swelling. Patient died at home on April 16th with a large growth in the posterior mediastinum, which had rapidly developed and invaded the spinal cord, causing complete paralysis and anæsthesia below the fifth intercostal space, with retention of urine. No other deposits could be detected. The parotid had enlarged considerably, but did not ulcerate or invade the mouth. No recurrence in operation scar. No autopsy was allowed.

Microscopic examination.—A small round-celled sarcoma, which is very necrotic. The nodule in the cord and the fluid withdrawn from the parotid were also sarcomatous.

CONCLUSIONS.

In this series of cases there are only seven of primary sarcoma of the testicle. This is a small number as compared with carcinoma, of which there are twenty-five cases. In most text-books on surgery it is stated that sarcoma is the commonest form of new growth. This is due to the fact that, until recently, the alveolar carcinomata were described as sarcomata, and that this group was also made to include many of the embryomata. Thus, in the hospital records, no fewer than thirty-five specimens are labelled sarcoma.

Every one of these seven cases is a small round-celled sarcoma, for, although case 29 shows many spindle-shaped and stellate cells, yet it is undergoing a myxomatous degeneration, in which condition the cells tend to assume an irregular shape. Even in this specimen, however, the round cells predominate. Krompecher goes so far as to say that a large round-celled sarcoma of the testicle does not exist, such growths being in reality endotheliomata. Several varieties of small round-celled sarcoma have been described. These are the lymphosarcoma, in which the cells are all of the same size, with large nuclei, and are contained in a delicate reticulum of connective tissue, and the angiosarcoma, which arises in the perivascular connective tissue around the blood and lymphatic vessels.

Origin.—Sarcoma begins in the connective tissue, both of the testicular stroma, and around the blood vessels, in which latter case we get an angiosarcoma. Its actual mode of origin is still open to doubt, namely, whether it begins in the fully-formed connective tissue cells, or in undifferentiated cells, which have lain dormant in the connective tissue and may possibly be used physiologically in the repair of the tissue. Under abnormal conditions, these take on an independent growth. They now do not find the necessary relations to the surrounding cells to enable them to differentiate into the fully-formed tissue, but grow in the undifferentiated embryonic form, giving rise to sarcoma tissue. The mere fact of its being an embryonic tissue explains why it is able to grow at the expense of and to destroy the adult tissue in which it originated. The appearance of the cells of a sarcoma is strongly in favour of this view.

Naked-eye appearance.—Very little need be added to what I have said when discussing carcinoma. The formation of cavities, owing to hæmorrhage and necrosis of the growth, seems to be more marked than in carcinoma. Mr. Jacobson also mentions that sarcoma does not involve the coverings of the testicle to such an extent as does carcinoma.

Bland Sutton points out the fact that sarcoma in paired organs in young people is often bilateral. Case 26 illustrates this point.

This case has been included in this series, since it is the only new growth of the epididymis in the museum.

History.—The average age at the time of operation is $34\frac{1}{2}$, the youngest being 6 and the oldest 72. This is somewhat younger than in carcinoma, in which the average is 43.

The average duration before operation is eleven months, as against one and a half years in carcinoma, the shortest history being five weeks and the longest three years. Case 27 had an enlarged testicle ever since he could remember. It is impossible to be certain as to its nature. Acute symptoms had only been present for three months.

Unfortunately, the after-history of only three cases is known. Of these, two died in hospital, and the third died within two months of the operation.

Malignancy.—It is usually stated that sarcoma of the testicle is very liable to disseminate by way of the lymphatics as well as the blood stream. Post-mortem examinations were performed on three cases. Of these one was a carcinoma, the others sarcoma. Briefly, the following appearances were found at the autopsy:—

i. Case 6 (carcinoma). Deposits were found in the retro-peritoneal, bronchial, and cervical glands. Metastases in both pleuræ, the thymus, the muscles of the back, and the œsophagus. No deposits in lungs, liver or kidneys.

ii. Case 26 (sarcoma). Deposits were found in muscles of back, penetrating into spinal canal; in interauricular septum, projecting into the right auricle; in both kidneys, and in the jejunum, in the neighbourhood of which deposit there were some enlarged glands.

iii. Case 27 (sarcoma). A large growth in the right inguinal region and half of pelvis, invading the bladder. Liver, kidneys, lungs, and *lumbar glands* healthy.

On comparing these three post-mortem examinations, it is very striking that the one which was a carcinoma showed extensive involvement of the lymphatic glands, whereas the sarcomata showed no such appearance.

Case 6 shows a very extensive involvement of the glands. The deposits under the pleura are no doubt produced by reflux of lymph after the blocking of the bronchial glands, which were sufficiently enlarged to obstruct the bronchus supplying a whole lobe of the lung. The invasion of the thymus can be explained by the same means. It is a lymphoid structure, and it is quite easy to believe that after blocking of the cervical glands the stream in the lymphatics supplying it may have been reversed. It is also possible that the deposits in the muscles of the back were produced by reflux of lymph-carrying cancer cells, or by solid rods of cells growing down the lymphatics.

Case 26, on the other hand, shows an extensive involvement of various tissues by the blood stream. There was a deposit in the right auricle. A few glands are said to have been enlarged in the mesentery of the affected loop of intestine. These no doubt drained that loop, and, as the growth had ulcerated into the lumen, in the absence of further evidence, it is legitimate to assume that the glands were enlarged from septic absorption and inflammation.

Case 27. It is very improbable that the deposit in the pelvis and inguinal region was glandular in nature. The lumbar glands were normal, as is stated in the report. The first gland into which the lymphatics of the testis drain lies at the level of the lower pole of the kidney. So if that gland was not affected, those lower down could not have been. It is conceivable that the tumour originated in the inguinal glands, but these are never invaded until very late in the course of the disease; long after the abdominal glands. It is therefore quite likely that this growth was deposited by the blood.

Three post-mortem examinations are, of course, not enough to dogmatise on, but I think it at least a suggestive fact that whereas, in the case of carcinoma, the dissemination was mainly, if not entirely, by the lymphatics, in those of sarcoma it was by the blood stream. It is therefore quite possible that sarcoma of the testicle, as of other organs, mainly disseminates through the blood.

I do not mean to state that sarcoma of the testicle never passes by way of the lymphatics. Occasionally it does so in other organs. I only wish to point out that it is possible it does not do so as often as is generally supposed.

The great malignancy of new growths of the testicle is no doubt in part due to the obscure and painless onset of the disease. Patients are not seen until it is too late. They usually present themselves for treatment when the tumour, owing to its large size, causes them inconvenience in walking, or when their general health becomes affected, when no doubt metastases have already occurred.

ENDOTHELIOMA.

CASE 33 (Surg. Reg. No. 920. Surg. Rep., 1901, Jacobson, 23).—Arthur G., 22, unmarried, was admitted for an enlargement of the right testicle, which had been noticed for ten weeks. No history of injury. It increased in size for six weeks, since when it has remained stationary. On admission, patient was a healthy-looking man. The right testicle was five times the size of the left. It felt fleshy. There was a lowly-rising boss at its upper and outer part. No pain except on manipulation. The cord was thickened. Lumbar glands not palpable. The organ was removed. After-history unknown.

Naked-eye appearance.—The growth was very vascular. At one spot several little buds were beginning to fungate through the tunica vaginalis.

Microscopical appearance.—The stroma is fibrous, with a good deal of myxomatous degeneration. Its cells are large, round, and spindle cells. There are numerous more or less elongated and slit-like large spaces, some of which are lined by cubical cells, whereas, in others, these become more columnar. Nowhere is there any separation of these cells from the stroma, as so generally happens in a carcinoma during the process of hardening. Red blood corpuscles can be seen in the spaces. We are therefore dealing with a hæm-endothelioma.

CASE 34 (Surg. Reg. No. 1381. Surg. Rep., 1902, Dunn, 190).—William H., 21, was admitted for an enlargement of the right testicle, which has been rapidly growing for three months. No history of injury. It has been painful the whole time. The pain is worse at present, and radiates to the groin. On admission, the right testicle measured three and a half by three inches. Its upper part was harder than the lower. The cord was not thickened. The tumour was removed. Patient writes in November, 1906, that he has been married for two years and has a child three months old. His general health is good.

Naked-eye appearance.—The specimen measures seven and a half cm. in length and six and a half cm. in breadth. The two layers of the tunica vaginalis are not adherent to each other. Under the tunica albuginea, in the lower part of the testicle, there is a large growth which is infiltrating the

albuginea. It consists of a soft, grey, new growth, with several hæmorrhages and large irregular spaces. The testicular substance is spread out as a thin layer over the upper pole of the tumour, from which it is separated by a space. Epididymis healthy.

Microscopic appearance.—The stroma is myxomatous. There are many irregular spaces lined by cubical epithelium, which is not bounded by a basement membrane. This is a typical endothelioma.

CASE 35 (Surg. Reg. No. 1958. Surg. Rep., 1904, Jacobson, 322).—James P., 30, a sergeant in the R.G.A., and a very fine-looking man, was admitted for a tumour of the left testicle. Ten years ago, after gymnastic exercises, he had pain in the testicle for two or three days, but cannot remember a definite injury. Since then the testicle has shrunk to half the size of the other and become very hard. Twelve months ago it began to grow in size, and has done so ever since. On admission, the left testicle measures four and a half by three inches. It is hard. There is a lowly-rising boss in its upper part. The epididymis is fused with the testicle. There is general fulness of the structures of the cord. No pain or tenderness. Left inguinal glands enlarged. The growth was removed. Since then patient has had a child born in August, 1905, a year after his discharge from the hospital. He saw Mr. Jacobson in April, 1906, who kindly informed me that he could make out no signs of recurrence.

Microscopical examination.—Composed of a myxomatous stroma, in which there are many spaces lined by one or more layers of cubical cells, which lie directly on the stroma. There are numerous clusters of these cells, at first sight resembling a carcinoma. Connective tissue can, however, be traced between them. These clusters in many parts have undergone mucoid degeneration at the centres, so that spaces are formed lined by one or more layers of cells containing in their lumen some mucoid debris. This is an obvious endothelioma, and closely resembles case 34.

CASE 36 (Surg. Reg. No. 2688. Surg. Rep., 1906, Fripp, 94).—Bernard F., 75, was admitted on May 30th, 1906, for an enlargement of the left testicle, which he had noticed five weeks previously. He gave a history of gonorrhœa fifty years ago, with a stricture ten years later; and a vague history of syphilis when a young man. On admission, the left testicle was enlarged, hard, and not painful. The cord was thickened and hard throughout. Nothing could be felt on rectal examination. There was a small left bubonocoele. Operation. The growth was removed. The lumbar glands were found to be enlarged. The incision was therefore prolonged to the level of the umbilicus. Large masses of glands were removed, but not all, since they extended as far as the kidney. Patient was discharged on June 22nd. He was re-admitted on July 21st for abdominal pain, vomiting, and severe constipation, which was relieved with enemata. His abdomen showed a hard mass to the right of the umbilicus, just below the costal margin, which was apparently not connected with the liver, and was diagnosed as being an intestinal metastatic growth. His liver was enlarged and soon reached to the umbilicus. He became jaundiced, developed signs of pneumonia, and died on August 20th. No autopsy was allowed.

Microscopic appearance.—The cells of this growth are large and epithelial in type, containing large nuclei with distinct nucleoli. They lie in alveoli, but connective tissue can be traced between the individual cells, and the alveoli are not distinct. At first this growth resembles a large round-celled alveolar sarcoma. In one part of the tumour, however, there are numerous slit-like lymphatic channels. The epithelium lining these shows transition from ordinary flat endothelium to rounded or cubical cells identical with those making up the rest of the growth. These cells lie directly applied to the stroma, which here, as everywhere, is reduced to the delicate fibrils between the large cells, and are in no instance separated off from it and projecting into the lumen, as so generally happens with an epithelial lining to a cavity during the process of hardening. There are also areas of mucoid degeneration. I therefore believe that we are dealing with an *endothelioma*, and that the alveolar appearance is produced by the change having originated in the endothelial cells of the small lymph capillaries. A gland, of which microscopic slides were prepared, shows the same structure.

CASE 37 (Museum No. 2111).

Naked-eye appearance.—The half of an injected testicle, about twice the normal size. The external surface is very irregular and presents several prominent nodules. The two layers of the tunica vaginalis are extensively adherent and infiltrated by new growth. The cut surface is composed of a mass of soft new growth, which forms incomplete lobules at the periphery. No traces of the testicular substance remain.

Microscopic appearance.—The stroma consists of large round and spindle cells, the former of which preponderate. The cells become condensed around the lymphatics, so that these vessels are lined by one or more layers of cubical cells without an intervening or internal layer of flattened endothelium. This tumour, which is labelled a carcinoma, is, therefore, a lymphatic endothelioma.

CASE 38 (Curator's Room No. 371).

Naked-eye appearance.—The whole testicle, which is enlarged to twice its normal size, is replaced by a spongy growth with small spaces and clefts on the surface. The growth is limited by the tunica vaginalis, the two layers of which are not adherent to each other. The epididymis and cord appear to be healthy.

Microscopic appearance.—The matrix is homogeneous and non-staining, and contains hardly any connective tissue cells. It has evidently undergone a high degree of myxomatous change. Numerous minute blood vessels can be seen in it, which, except for rather thick walls, show no change. The whole of the stroma is permeated by small lymphatic capillaries. In some of these the endothelium is flattened, whereas in others it becomes more and more cubical, so that the majority of these spaces are filled with a cluster of from four to eight cubical cells, which lie directly against their walls and have no external lining of endothelium. In several of the spaces, cut longitudinally, the transition can be made out from flattened to cubical endothelium. We are, therefore, dealing with a lymphatic endothelioma.

CONCLUSIONS.

In this series of cases there are six of endothelioma of the testicle. They present a microscopical appearance intermediate in character between that of carcinoma and sarcoma. The former they resemble in the formation of the cells, which are epithelial in type, having clear nuclei with distinct nucleoli. No intermediate forms can be made out between them and the connective tissue cells. There is also distinct alveolation. They resemble a sarcoma in that connective tissue can, in most places, be traced between the individual cells, and in that, owing to these cells arising from, and thus, in a measure, replacing the endothelial lining of the vessels, their connection with the stroma is much more intimate than in carcinoma, there never being any shrinking away of the cells from the connective tissue, as is often seen in carcinoma as the result of the hardening process. On a superficial examination the cells, therefore, seem to grow out from the stroma. Myxomatous degeneration, which in many cases is far advanced, is an important characteristic of these growths. Krompecher classes the large round-celled sarcomata with the endotheliomata. He points out that in them the essential cells of the growth are always sharply bounded from the connective tissue and adventitia of the vessels, which is against their being of connective tissue origin. He shows that if an endothelioma arises in the small lymph-capillaries it produces the appearance of a network of large cells, the intervening collapsed vessel wall being invisible, in the meshes of which the stroma is to be seen. He makes out endotheliomata to be the commonest form of new growth in the testicle (excluding the embryomata). From what I have been able to find, however, he seems to go too far.

Origin.—Endotheliomata are supposed to arise from the endothelial lining of the lymphatic and blood vessels. In the former case they are known as lymph-endotheliomata, in the latter as hæm-endotheliomata. Case 33 is the only hæm-endothelioma in this series. The flattened endothelial cells become cubical, and even columnar, and, by division, give rise to many layers, which

may obliterate the lumen of the vessel from which they originate. This change in form of the endothelial cells can also be observed during the process of inflammation, in which all the fixed cells of the part enlarge and proliferate. The assumption of a cubical shape must be regarded as a regressive change, bringing the cells nearer to their embryonic form. They become less differentiated, but can never undergo a change into epithelium, for which they are so frequently mistaken. The formation of several layers of cells makes their resemblance to epithelium even greater. Such an appearance is produced in case 36, which in many places shows small alveoli.

History.—The average age of the patients at the time of the operation is 37. Three patients were between 21 and 80. One was 75 years old. These growths can, therefore, begin at any age, but are, doubtless, if we consider the age incidence of endothelioma in other organs, much more common in early than in late life. The average duration of the disease was about four months; the shortest being five weeks and the longest a year.

Case 35 gave a definite history of an attack of orchitis ten years before, with subsequent fibrosis and atrophy of the testicle, and the development of active growth nine years after the beginning of the trouble.

One patient is alive four, and another two, years after the operation. This points to a comparatively benign course of the disease. On the other hand, case 36, who was 75 years old, and had noticed the tumour for only five weeks before its removal, died within three months of the operation, with extensive involvement of the lymphatic glands within the abdomen. In this patient the disease ran a very rapid course to a fatal termination. This may be due to his age, and consequently lowered resistance to the spread of the growth.

In the only case in which metastasis occurred, it was shown to have taken place in the lymphatic glands. This is in accordance with what one would expect, as this growth had originated in the endothelium of the lymphatics.

EMBRYOMA.

The specimens of new growth of the testicle which still remain to be described all show derivatives of one or more of the primary embryonic layers; the epi-, meso-, and hypoblast. A typical example should show derivatives of all these layers, but in many instances one, or even two, may not be found. The reason of this absence may be due either to the fact that the layer in question has been suppressed by the growth of the other layers, or that it is present in such minute quantities that it has not been observed in the sections examined. It may be well here to emphasize the great importance of examining under the microscope as many sections taken from different parts of the tumour as possible, since it is often not possible to arrive at a correct diagnosis of the nature of the new growth after having examined a section taken from only one part.

CASE 39 (Surg. Reg. Nos. 2292, 2316, 2405. Surg. Rep., 1905, Golding-Bird, 349).—Thomas W., 30, was admitted into Guy's Hospital on May 29th, 1905, for a swelling of the left testicle. He is married, but has no children. He has had occasional slight hæmoptysis. In January, 1905, he injured his left testicle with a packet. He suffered great pain for several days. The left testicle began to increase in size until May 22nd, when the swelling burst on the anterior aspect of the scrotum, and a considerable quantity of blood-clot and matter was discharged. He complains of severe pains at times. On admission, patient's temperature was 100° F. The skin of the scrotum was inflamed, and there was a discharging sinus. The left testis was large, conical, with a bossy surface and evidence of fluctuation. It was painful on being manipulated. Testicular sensation was present in some parts of the swelling. The cord was not thickened. Inguinal glands and vesiculæ seminales enlarged. Lumbar glands not palpable. May 31st: The sinus was enlarged and scraped. Blood and some doubtfully tubercular matter were removed. Also a piece of tissue resembling testis was preserved for microscopic examination. The wound was packed with gauze. The report on this piece of tissue was: "Hæmatoma with some testicular substance."

Patient did well until June 15th, when the testis again began to enlarge and the skin to inflame. Therefore, on June 19th, the mass, together with the inflamed skin, was removed, and from the naked-eye appearance of the growth a sarcoma diagnosed. The wound healed well and patient was discharged on July 6th.

Microscopic report.—Columnar-celled carcinoma. Three weeks after leaving the hospital the growth recurred locally, and patient was re-admitted on August 23rd with the left side of the scrotum filled with a lobulated discharging growth. It was very hard and adherent to the skin. On the 25th the left side of the scrotum, with the growth contained in it, was removed and the skin sutured. Under the anæsthetic no enlarged lumbar glands could be

felt, but one about the size of a walnut was found over the external iliac artery. Primary union. Discharged September 19th.

Microscopic report.—Columnar-celled carcinoma with hæmorrhage.

On making inquiries I find that patient died on January 10th, 1906, at home. I can gather no particulars as to his history before death.

Three microscopic slides were examined, taken from patient at different times. I will now describe these in order:—

(1) May 31st (No. 2292).—The main part of the slide consists of blood-clot. This does not, however, belong to an extravasation of blood into a large space, such as the tunica vaginalis, but has occurred into the connective tissue of the new growth, since in all parts of the section the structures now to be described are seen in a very good state of preservation.

The *mesoblastic stroma* consists of young connective tissue, with a large number of small round cells, in places so abundant as to present the appearance of a small round-celled sarcoma. Everywhere there are numerous cysts and spaces. Some of these cysts are filled with blood-clot, their epithelium is lost, or only traces of it remain. Others have a well-marked epithelial lining. Some unstriped muscle is to be seen. The following kinds of epithelium are visible:—

Epiblast.—Solid rods of *stratified epithelium*. The outermost cells are columnar with rod-shaped nuclei. The inner cells become rounded with a clear cell body and distinct nuclei. This epithelium resembles that of the skin closely, showing its different layers. In one or two of these spaces the central cells have become cornified, forming *epithelial pearls*, still surrounded by several layers of rounded cells and an external layer of columnar cells resembling the rete-Malpighii of the skin. In other cells dark granules of eleïdin are found.

Hypoblast.—Numerous cysts lined by tall *columnar* or *cubical* epithelium. In many of these spaces the epithelium has been shed into the lumen as long rods, made up of several cylindrical cells. I can see no goblet cells. There are also numerous tubules lined by a columnar epithelium with a central lumen. These are in places collected into groups, so as to resemble *glands*.

We therefore see that this section contains derivatives of the three embryonic layers.

(2) June 19th (No. 2316).—Here there is a rather scanty stroma of young connective tissue. It forms a wide-meshed network, in the spaces of which there lie large masses of partly spheroidal, partly columnar cells. Most of these masses present numerous necrotic areas in which the cells have refused to stain. This growth closely resembles a rapidly-growing *carcinoma* of the pylorus. In the stroma small collections of *gland-acini* can be seen. There is a large piece of the original testicular tissue to be seen. Here the testicular tubules are degenerated, being composed of little else than a thick hyaline tunica propria, inside some of which a few degenerated epithelial cells can be seen. Nowhere is there any trace of active growth in the epithelium of the seminal tubules.

This section, then, shows structures derived from the mesoblast and the hypoblast, the epiblast not being represented. It also shows that the testicular tubules take no active part in the formation of the neoplasm.

(8) August 25th (No. 2405). Here the section consists of one large mass of columnar carcinoma cells. Into the lumina of these masses of cells blood has been extravasated everywhere, giving in many places an appearance like thyroid tissue, with the blood substituted for the colloid. In many places the extravasation has completely destroyed the cells, so that nothing but a blood clot remains. In one part the growth can be seen to be invading the thickened tunica albuginea. In another part testicular remains are distinguishable, even more degenerate than in the last section.

This section, therefore, only contains derivatives of the *hypoblast*.

If we compare these sections with each other we see a very interesting change. In No. 1, derivatives of the three layers can be made out, the mesoblastic stroma being greatly in excess. There is no evidence of any cancerous change. This corresponds with the clinical history. The growth had taken five months to grow to its present size, and the fact of its bursting through the skin at last may be ascribed to the tension and inflammation set up by the large effusion of blood that was present, since it is a most unusual behaviour for a growth of the testis to fungate. No. 2 had grown in a few days. Its appearance is very malignant, but there is still some stroma with non-malignant-looking gland-acini left. The growth of No. 3 is again very rapid, and the section resembles a highly malignant columnar-celled carcinoma. Accordingly we find that it destroyed life in less than five months.

We therefore see that in an embryoma, which contains the three embryonic layers, and is not necessarily malignant, one layer may grow and acquire malignant properties at the expense of the other two. In this case it was the hypoblast. In other cases it may be one of the other two layers.

If the first of these three sections had not been cut and examined, this specimen would have been called a columnar-celled carcinoma of the testicle. It was only by examining the earliest section, in which the three embryonic layers are preserved, that it became possible to arrive at a correct diagnosis.

It may be well to point out that the stratified epithelium seen in the first section closely resembles that of the skin. A rete-Malpighii, stratum granulosum, and stratum corneum, can be readily made out.

The stroma has a cellular, embryonic appearance. It contains many spindle and stellate cells, and resembles very closely embryonic connective tissue.

CASE 40 (Museum No. 2106. Insp., 1861, 6. Published by Mr. Durham in Trans. Path. Soc., 1862, vol. xiii., p. 166).—Godfried W., 19, had his testicle removed by Mr. Durham in 1861. He suffered great pain across the abdomen, which continued after the operation. He died suddenly after dinner, on January 5th, 1862. At the post-mortem examination the body was not wasted. No disease was to be seen externally. The lungs were healthy. The liver contained one deposit of new growth. A large mass of malignant lumbar glands occupied the spine and involved in them were the aorta and vena cava.

Naked-eye appearance.—A testicle somewhat enlarged and laid open to show the whole of its substance occupied by nodular masses of a new growth, which contains a few smooth-walled cysts. These nodules are separated from each other by strands of white fibrous tissue. The tunica vaginalis is thickened, and its layers are extensively adherent. No remains of the secreting substance of the testicle are to be made out. The epididymis is incorporated in the new growth.

Microscopic appearance.—Sections were cut from several parts of the new growth. This is very necrotic. The stroma is represented mainly by thin trabeculae of a firm consistence, which in a few places becomes more cellular, and resembles embryonic connective tissue. This, then, is all there is to be seen of the *mesoblast*. The *epiblast* is represented by a few rods of stratified epithelium, the innermost cells of some of which have become extensively cornified, so that cell-perls are formed. These epiblastic derivatives are few and far between. The main mass of the growth is made up of a tissue like a columnar-celled carcinoma, which closely resembles the second slide described in the last case, and is obviously derived from *hypoblast*. Many remains of testicular tubules are to be seen. At the margin of the new growth they become compressed and atrophied by the cells of the new growth, which seem to spread by the lymphatic channels in the intertubular stroma. I have not been able to satisfy myself that the cells of the neoplasm make use of the testicular tubules in order to spread along them. One can see many tubules squeezed almost flat by masses of new growth outside them, which seems to show that they are merely compressed and then eaten away by the neoplasm.

This case, then, contains derivatives of all the blastodermic layers. The hypoblast has, however, taken on an active growth at the expense of the other two layers, and has assumed malignant properties. It has produced metastases and destroyed life in the same way as a carcinoma.

CASE 41 (Museum No. 2115. Surg. Rep., vol. clxiii., No. 107).—John A., 47, was admitted on March 1st, 1893, for swelling of the left testicle. When 18 he had an attack of gonorrhœa. He is married and has several children. Three months before admission he bruised his left testicle slightly with the saddle when on horseback. Pain and swelling of the testicle commenced one month before admission. On admission, the left testicle was three times the natural size. Its surface was nodulated. There was no pain. The cord was thickened. The testicle was removed, and patient made an uneventful recovery. After-history: On January 31st, 1903, patient was killed in a carriage accident. Up to the time of his death he had been in the best of health.

Naked-eye appearance.—The testicle is enlarged to four times its natural size, and is laid open to show, in its lower part, an encapsuled new growth, about three times the size of the natural organ. This growth is dotted over with numerous small cysts, some of which are lined by a definite mucous membrane, and most of which contain secretion. The growth itself is soft and hemorrhagic. It has fungated through both layers of the tunica vaginalis, which are adherent to each other.

Microscopic appearance.—The stroma makes up the greater part of all the sections examined. It is richly cellular, and in places myxomatous. Large hæmorrhages have taken place into its interior. It closely resembles embryonic connective tissue, and is characteristic of the *mesoblast*. One small nodule of cartilage was observed in it. The *epiblast* is represented by one or two small spaces lined by stratified epithelium. The *hypoblast*, which is far in excess of the epiblast, consists of tubules and cysts lined by a tall columnar epithelium, many of the cells of which have assumed the shape of goblet cells. This epithelium is bounded externally by a basement membrane. Nowhere does it show any tendency to burst through this membrane. A cyst is present lined by both stratified and columnar epithelium.

Here, again, are represented derivatives of the three blastodermic layers. The mesoblast is in excess. Although at first sight it bears a resemblance to a sarcoma, yet this appearance is characteristic of embryonic connective tissue. The epithelial elements show no signs of malignant growth. In accordance with this is the after-history. The patient was killed accidentally ten years later, and there had never been any signs of recurrence.

This case was published by Mr. Bryant in the Transactions of the Pathological Society, 1858, vol. ix., p. 340, "Medullary Cystic Disease of the Testicle." The following account is given of the history of the case.

CASE 42 (Museum No. 2121).—John S., 26, was admitted under Dr. Cock on April 17th, 1858. Appearance pale and cachectic. Health indifferent. Since boyhood, after retaining his urine for some time, his right testicle

retracted and disappeared from the scrotum, causing at times great pain. Gonorrhœa six years ago. Chancre on penis one year ago, but no secondary symptoms. About one year ago, without any blow or known cause, his right testicle began to enlarge, unattended by pain. Since then it has gradually increased in size, and on admission it was about four inches long in its longest diameter. Painless, and could be manipulated without inconvenience. Oval, slightly flattened, fluctuated in places. Inguinal glands slightly enlarged. For the last year he had experienced flying pains down the right leg. Castration on April 20th. After-history unknown (Trans. Path. Soc., 1882, vol. xxxiii., Supplement).

Macroscopic appearance.—Surface smooth, and free from adhesions. Epididymis wasted with several cysts, two of which were pedunculated. On section, the testicular substance had entirely disappeared, being replaced by a growth with distinct alveolar stroma and numerous cysts, varying in size from a walnut to a millet seed. Some were filled with clear serum, others with a bloody or tenacious fluid, while others contained a soft pulpy growth, composed entirely of nuclei and cells, and presenting the appearance of medullary cancer. Some cysts appear to be lined by a definite mucous membrane. Mr. Bryant concludes that we are dealing with a case of cystic disease of the testicle, on to which was grafted a medullary disease.

Microscopic appearance.—The sections examined are very necrotic.

Epiblast.—One tubule lined by stratified epithelium, most of the cells of which have become cornified.

Mesoblast.—The stroma is in places firm. In others it is cellular and myxomatous. In others there are large areas resembling a small round-celled sarcoma. Again, there are areas closely resembling an endothelioma, there being spaces lined by cubical or columnar cells which firmly adhere to the surrounding stroma.

Hypoblast.—Tubules lined by tall columnar cells, separated from the stroma by a basement membrane. The greater part of the hypoblast has taken on a growth closely resembling a columnar-celled carcinoma, so that many fields only show these cells, and might easily be mistaken for this kind of growth.

In this specimen there are present derivatives of all the blastodermic layers. The hypoblast, and possibly the mesoblast, has assumed a malignant change. It is a pity that nothing is known about the after-history, as it would be very instructive to compare it with that of Case 41.

CASE 43 (Museum No. 2138).—This tumour was removed by Sir Astley Cooper, and regarded by him as a specimen of "tubular" disease of the testis, the cysts being supposed to arise from dilatation of seminiferous tubules.

Macroscopic appearance.—The tumour is the size of a fist. The tunica albuginea is thickened and the surface somewhat nodular. There are traces of testicular substance to be seen at the periphery of the growth. The growth itself is fairly firm and smooth, with fibrous trabeculae intersecting

each other; there are also numerous small cysts scattered about and a few large ones near the tunica albuginea.

Microscopic appearance.—I have been able to examine sections taken from the whole cut surface of the growth. These show the following structures:—

Epiblast.—There is a collection of cysts lined by *stratified epithelium*. Some of these are entirely filled by these cells, whereas in others the cells have become detached and degenerated in the centre, leaving a lumen filled with the debris of cells. There are also solid rods of epiblastic epithelium, in some of which *epithelial pearls* have been formed. Several circumscribed nodules can be seen, in which there are large cells with distinct nuclei, resembling *ganglion cells*, and smaller cells resembling transverse sections of *nerve fibres*. These nodules are occupied by connective tissue, in the spaces of which the above-mentioned cells are seen lying. I have compared these nodules with a section of a *spinal ganglion*, and they closely resemble it.

Mesoblast.—The stroma is in places dense and fibrous, but in the greater part of the tumour it is very soft and myxomatous. In the dense part numerous *unstriated muscle-fibres* can be seen, especially around some of the cysts. The myxomatous areas contain round, spindle, and branching cells. These may be slender and very long, or of the shape of myocardial cells, or fusiform, or round. They are striated muscle fibres. Neumanu regards the fusiform cells as being embryonic, and the round cells as being misshapen muscle-fibres. Several small areas of *cartilage* are scattered about.

Hypoblast.—Some of the largest cysts are lined by tall *columnar epithelium* with numerous *goblet cells*. These often project into the lumen as villi, which are formed by out-growths of connective tissue. Around these cysts bundles of plain muscle-fibre can be seen, so that a distinct resemblance to the intestinal mucous membrane is produced. There are also smaller spaces filled with *spheroidal cells*, and large areas in which these cells have run wild, there being no limit to the masses formed by them, so that there is an appearance of an *encephaloid cancer*.

Numerous *testicular tubules* can be seen. Those near the new growth are flattened; their tunica propria is thickened and their cells degenerated. Those farthest removed from the growth appear healthy, and in some of them the heads of spermatozoa can be seen. I could make out no increase of the interstitial cells.

This specimen is, in the museum catalogue, labelled a rhabdomyosarcoma. The section preserved in the museum has been taken through the myxomatous part of the growth and shows nothing but sarcomatous cells and striated muscle fibres. I suspected the specimen of being an embryoma, since numerous cysts are to be seen on its surface. I was able to examine a thin slice removed from the whole of the cut surface of this tumour and to demonstrate the presence of *all three germinal layers*. This proves that

we are not dealing with a rhabdo-sarcoma, but with an embryoma, in which there happens to be a very large development of striated muscle. We thus see the importance of examining as many parts of these tumours as possible, and of not being content with merely one small section. This tumour must be nearly a century old, and in consequence it was very difficult to stain the sections. Methylene blue was the only stain I could get them to retain.

This tumour was removed from a patient two years old. I can find no other particulars.

CASE 44 (Guy's Hospital, Museum No. 2122).

Macroscopic appearance.—The specimen is a slice of the original tumour. It is pear-shaped, the thin end during life occupying the inguinal canal. It is firmly adherent to the scrotum. The original tumour must have been very large.

Histology.—There are no cysts in the section. *Mesoblast:* The general stroma has the appearance of a *spindle-celled sarcoma*. There are many *plain and striated muscle fibres*. These latter have large nuclei and are round, spindle-shaped, and branching. The striation is obscure. There are collections of round cells resembling *lymphoid tissue*. *Hypoblast:* Several spaces lined by a very necrotic columnar epithelium.

It may well be urged that we are dealing with a rhabdo-sarcoma. I have, however, included this case in the group of embryomata, chiefly on the evidence furnished by the last case. Here the section preserved showed a rhabdo-sarcoma, and it was not until other sections were examined that its true nature was discovered. We also see plain as well as striated fibres. I therefore think it is more correct to assume that this tumour is an instance of the common embryoma of the testicle, and not one of a very rare form of growth, the existence of which has been doubted by some observers.

CASE 45 (Museum No. 2123).—Nothing is known of the history of this specimen.

Naked-eye appearance.—The testicle measures five inches in length, and is uniformly infiltrated with a new growth, which forms prominences on its surface. The cut surface is granular and necrotic, and contains much extravasated blood. Close to the thickened tunica vaginalis there is a space with collapsed walls, the edges of which show a peculiar brown stain. The tunica vaginalis is obliterated.

Microscopic appearance.—The bulk of the tumour is made up of intersecting and branching strands, and whorls of unstriped muscle fibre.

Included in this formation are several large islands of fibrous tissue, which, in some places, has become myxomatous. The cyst with the collapsed walls is separated from this part of the tumour by a layer of firm, fibrous tissue. This tissue, on being traced towards the lumen, becomes more open and cellular, and among its cells a large number of different kinds of cells are to be seen. Many of these are very large, round or oval, or pear-shaped, with a large vesicular nucleus. They are obviously ganglion cells. Others are smaller, round or oval, and appear to represent nerve cells and fibres. Many of these cells contain a dark-brown granular pigment. Their meaning becomes obvious on remembering that the retina possesses a layer of pigment cells. This structure may then be taken as representing a rudimentary eye, in which the ganglion cells and pigmented cells have become arranged in the utmost confusion.

In this specimen, therefore, there are derivations of only the epi- and the mesoblast. Both these layers have assumed a higher degree of differentiation than is usual in embryomata of the testicle. The epiblast forms a rudimentary eye, and the mesoblast is almost entirely represented by unstriped muscle tissue.

CASE 46 (Museum No. 2131).—This specimen was presented by Mr. Aston Key. There is no record of its history. The tumour is laid open to show the organ occupied by partly encapsuled masses of growth, which contain many cysts, some of which show a definite mucous membrane. The surface is nodular. The epididymis appears to be healthy.

Microscopic appearance.—

Epiblast.—Several cysts are to be found, lined by stratified epithelium. There are masses of spheroidal cells surrounding a cavity lined by a single layer of columnar cells, resembling the spinal cord.

Mesoblast.—The stroma is composed of round cells, and is myxomatous and hæmorrhagic in places.

Hypoblast.—There are cysts lined by *cubical* or by *columnar ciliated epithelium*. There are also structures resembling *gland acini*, lined by cubical epithelium.

In one cyst both stratified and ciliated epithelium can be seen side by side. Here again, as in the other cases, the line of junction of the two is quite abrupt, a ciliated cell immediately adjoining several layers of squamous cells, there being no cells of intermediate character.

This specimen contains derivatives of all the embryonic layers. It is unfortunate that nothing is known about the after-history, since none of the layers have undergone a malignant change.

CASE 47 (Museum No. 2132).—This tumour, which is labelled a cystic chondro-carcinoma, was removed by Mr. Cock in 1866.

Naked-eye appearance.—The tumour is four inches in length. The testicle is replaced by a new growth of varied character and consistency. In the upper part it is fairly firm and homogeneous. Separated from this by a capsule are masses of soft hæmorrhagic material surrounded by a fibrous capsule in which there are numerous nodules of cartilage and some cysts. There are some large cysts filled with a caseous material.

Histological appearance.—

Epiblast.—Numerous cysts lined by many layers of *stratified epithelium*, which in places have undergone a horny change, forming *epithelial perls*. Around some spaces, which are occupied by these cell-perls, there are large multinuclear giant cells, which can be seen eating into and removing the horny epithelium. This appearance was first observed by Wilms. There are some large connective tissue cells in the stroma near these giant cells, which probably, by their growth and confluence, go to form them. The epithelial perls attacked have in each case spread to the periphery of the space in which they were produced, so that there are no living epithelial cells between them and the stroma. They no doubt irritate the connective tissue, with the result that phagocytic giant cells are formed from the connective tissue cells. These remove the irritating body. A well-formed developing *tooth* with enamel and dental sac can be seen. It is, however, not related to any cartilaginous nodule.

Mesoblast.—The stroma is in places dense and fibrous, in others delicate and loose, and showing extensive mucoid areas. Some places are very hæmorrhagic. There are nodules of hyaline *cartilage*, and also collections of round cells, or *lymphoid follicles*.

Hypoblast.—There are numerous cysts lined by a *columnar ciliated epithelium*. There are also areas presenting the appearance of a *spheroidal-celled carcinoma*. There are also several acini lined by more or less columnar cells, resembling *glands*.

This is a most interesting specimen. Not only are there many derivatives of all the blastodermic layers, but a reaction to foreign bodies, similar to that which occurs in the normal body, is shown. The dead epithelial perls must be regarded as foreign bodies, as mild aseptic irritants. The connective tissue of the new growth reacts to these irritants by the formation of giant cells.

There can be little doubt that this tumour recurred, since the hypoblast has undergone a malignant proliferation. It is, therefore, a great pity that nothing is known about the after-history of the case.

CASE 48 (Museum No. 2133).

Macroscopic appearance.—The growth is three and a-half inches in length. It presents the appearance of a mass of translucent milky blue matter, consisting of cartilage, traversed by strands of a firmer white connective

tissue. At the lower part of the tumour there is a mass of shreddy new growth which is very necrotic. The tunica vaginalis is thickened.

Histological appearance.—There are no epiblastic elements.

Mesoblast: The greater part of the section consists of hyaline cartilage. Between the nodules formed by it there are thin strands of connective tissue, the cells at the periphery of which can be seen to become surrounded by the cartilaginous matrix.

Hypoblast.—There are some masses of spheroidal cells in the stroma, presenting an alveolar arrangement in several places.

This specimen, in which derivatives of only the meso- and hypoblast are present, is of interest in that its main part is composed of hyaline cartilage. As will be pointed out later, it was thought at one time that a pure enchondroma of the testicle exists, and that it may even disseminate. That this is not so, in this case at all events, is shown by the presence of hypoblastic structures.

CASE 49 (Museum No. 2134).—History unknown. The tumour, which lies beneath the tunica albuginea, consists at its periphery of homogeneous material with a few cysts. The centre is less dense and contains a large number of cysts. It is partially surrounded by a fibrous capsule, beneath which there is extensive degenerative softening. The tunica vaginalis is thickened and adherent.

Microscopical appearance.—Two sections are preserved. The first consists of a soft connective tissue, resembling a myxo-sarcoma, with no epithelial elements. The second contains derivatives of the epiblast in the form of cysts lined by a stratified epithelium, transitional in type. The mesoblastic stroma is dense and fibrous, and contains a few nodules of cartilage. No derivatives of the hypoblast could be seen.

This is the second case in which no hypoblastic tissues were found. Generally, when a layer cannot be demonstrated, it is the epiblast. This is, however, quite a different thing to saying that the hypoblast is absent. If more sections could be examined, there is little doubt that it would be found.

CASE 50 (Museum No. 2135. Surg. Rep., vol. lx., No. 69).—Alfred C., 29, was admitted on May 22nd, 1890, for an enlargement of the left testicle. The left testicle had always been larger than the right, but not harder. Nine years ago this testicle was injured by a cricket-ball, and was painful and tender for a few days. Two months before admission, after much walking, patient felt pain in it. He found it to be large and hard. It increased in size for a week; since then it has remained stationary. On admission, the left testicle was oval, about the size of a tennis-ball, and very hard. The cord was thickened. On May 27th the organ was removed.

Patient made a good recovery and left the hospital on July 2nd. A post-card, which I sent to patient's address in October, 1906, on the chance of gaining some information about his after-history, was returned by the Post Office as "unknown."

Macroscopic appearance.—The tumour is two and three-quarter inches in diameter. At the upper part there is a thin layer of testicular substance. The growth is encapsuled, and on section has a convoluted structure and contains many cysts, some of which are lined by a thick mucous membrane, and pieces of cartilage. The tunica vaginalis is adherent.

Histologically—

Epiblast.—The majority of the cysts are lined by *stratified epithelium*, which in some cysts is becoming cornified. There are also some *cell-perls*.

Mesoblast.—The stroma is composed principally of a loose myxomatous tissue, with many small spindle cells. There are some bundles of *unstripped muscle fibre*. No cartilage is present in the section, but it is obvious to the naked eye in the tumour itself.

Hypoblast.—In one place there is a collection of *spheroidal cells* arranged in alveoli.

We here again find all three blastodermic layers represented. The ectoderm in the section examined preponderates over the entoderm.

CASE 51 (Museum No. 2136).—William B., 30, was admitted under Mr. Cock, in 1862, for a painful swelling of the testicle, which had been observed for six months. His general health was not affected. The tumour is three inches in length. The cut section shows bands of connective tissue and numerous translucent areas of cartilage, and a few small cysts lined by a definite mucous membrane. The surface is nodular, and the two layers of the tunica vaginalis adherent.

Microscopic appearance :—

Epiblast.—Numerous cysts are lined by *stratified epithelium*. In some the cells have proliferated so as to entirely fill up the lumen.

Mesoblast.—The stroma is composed of fibrous tissue. There are numerous circular nodules of *hyaline cartilage*. There are many bundles of *unstripped muscle*, arranged in two layers, an internal circular and external longitudinal, around many of the cysts and nodules of cartilage.

Hypoblast.—The majority of the spaces are lined by *columnar epithelium*, with numerous goblet cells.

This tumour, which contains derivatives of all three blastodermic layers, is singularly non-malignant in appearance. All the tissues are fully differentiated, and well-formed mucous membranes result, which are evident to the naked eye. The cysts, lined by columnar epithelium and surrounded by two layers of unstripped muscle, closely resemble the intestine.

CASE 52 (Museum No. 2137).—Taken from a child of twenty-two months, whose testicle was noticed to be enlarged at birth. It increased rapidly during the three months preceding its removal by Mr. Foster, in 1864. The tumour is one and a half inches in length, and consists of a uniform soft white growth, which is covered by the tunica vaginalis.

Microscopic appearance.—No epiblastic derivatives found in the section examined.

Mesoblast.—The stroma is in places fairly firm, and resembles connective tissue. In others it is much softer, so as to present the appearance of a myxo-sarcoma.

Hypoblast.—Spaces lined by *columnar epithelium*, which, in places, has taken on a malignant growth, invading the connective tissue. There is a good deal of testicular substance visible, which is much compressed and atrophied.

In this tumour we only find derivatives of two layers, the epiblast not having been found. The hypoblast has taken on an active growth, which, no doubt, accounts for the rapid enlargement during the three months before removal. Unfortunately, nothing is known about the after-history.

CASE 53 (Museum No. 2139).—Joseph W., 44, had noticed a painless enlargement of his testicle for some months. When removed it weighed two pounds. It was presented by Mr. Hilton. The tumour is five inches in length. The cut surface shows a very dense white fibrous tissue with many irregular cysts, in most of which a thick mucous membrane can be made out. The tunica vaginalis is adherent.

Microscopic appearance:—

Epiblast.—There are many cysts lined by *stratified epithelium*.

Mesoblast.—The stroma is a loose myxo-sarcoma, most of the cells of which are large spindle cells. There are numerous strands of *unstriated muscle-fibre*. No derivatives of the hypoblast were found.

This section only contains *epi-*, and *mesoblast*, but there can be no doubt that *hypoblast* exists in other parts of the tumour, or has existed at some previous period.

CASE 54 (Museum No. 2140).—This tumour was removed from a young epileptic patient. It is four inches in length and entirely composed of new growth. The cut surface is in parts hæmorrhagic and necrotic, and shows a few cysts. The tunica vaginalis is partly adherent.

Histology:—

Epiblast.—Several cysts are lined by *stratified epithelium*. There are also some *cell-perls*.

Mesoblast.—The stroma is a myxo-sarcoma. There are many *unstriated muscle fibres*. No cartilage in section.

Hypoblast.—Several acini filled with *spheroidal epithelium*.

This tumour contains all three blastodermic layers.

CASE 55 (Museum No. 2141).—This case was published by Mr. Durham in the Transactions of the Pathological Society, vol. xiii., 167, as "Cystic disease of the testicle." It is from a man of twenty-two, whose testicle was removed in 1861. The enlargement was first noticed when patient was five years old. It was tapped on two occasions and a small quantity of mucoid fluid removed.

Macroscopic appearance.—The tumour is three and a half inches in length. The surface is nodular. It is opened to show numerous cysts, varying in size and separated by dense fibrous tissue and cartilage. Many of the cysts are lined by a thick mucous membrane. Some contain a caseous, others a shreddy and horny, secretion.

Microscopic appearance :—

Epiblast.—Solid rods and small cysts lined by stratified epithelium.

Mesoblast.—The stroma is very fibrous. It contains nodules of cartilage and strands of unstriped muscle.

Hypoblast.—There are several large cysts lined by a very tall columnar ciliated epithelium with large round granular nuclei. Between these cells there lie smaller ones of a fusiform or rounded shape. In the neighbourhood of these cysts there are very striking collections of gland acini, which bear a strong resemblance to mucous glands. In the cells of these acini the nuclei are small and lie near the surface, whereas the protoplasm is swollen and clear and appears to be charged with mucin. There are also structures which resemble ducts; these are lined by a cubical epithelium with darkly-staining protoplasm and large round nuclei.

Derivatives of the three layers are here to be made out. The cysts lined by ciliated epithelium, with mucous glands in their vicinity, bear a strong resemblance to the respiratory mucous membrane.

Case 56 (Surg. Reg. No. 327).—Charles M., 25, was admitted into Bright ward in December, 1898. The testis was removed. I have been unable to ascertain any facts about the history, or the naked-eye appearance of the growth. There is a microscopic slide preserved in the collection in the Surgical Registrar's room. It shows the following structures :—

Epiblast.—There is a cyst lined by *stratified epithelium*, and numerous *cell-perls*.

Mesoblast.—The greater part of the stroma is *fibrous*. In places it has undergone *myxomatous* degeneration, whereas, in others, it is very cellular, resembling a *sarcoma*. There are several nodules of *hyaline cartilage*, some of which are beginning to be calcified in their central parts. Some small nodules are seen, consisting of large cells with a very definite lining to each cell, and a distinct nucleus. The cell protoplasm does not take the stain. This is, as Shattock has pointed out, probably *embryonic cartilage*. There are many areas closely resembling an *endothelioma*, the spaces of which are lined by a layer of cubical cells without a basement membrane. The stroma here is peculiarly *myxomatous*.

Hypoblast.—There are numerous cysts lined by a tall *columnar epithelium*. The lumen of these cysts contains a mucoid matter, which undoubtedly represents the secretion of this epithelium. As this secretion increases it distends the cyst, and the lining epithelium, owing to the pressure, becomes more and more flattened. There are also some small spaces lined by columnar epithelium, which resemble *gland alveoli*.

In this specimen there are present derivatives of all the blastodermic layers. The mesoblast is in excess, and has undergone an endotheliomatous change. With the possible exception of these areas of endothelioma, there is nothing malignant about the slide.

CASE 57 (Surg. Reg. No. 931. Surg. Rep., 1901, Jacobson, 56).—William C., 40, was admitted into Guy's Hospital on January 7th, 1901, for a swelling of the right testicle. Patient is married and has seven children. He can remember no definite injury, but states that he strained himself on lifting a weight some time before the present trouble began. He noticed an enlargement of the right testicle six or seven months before admission. It had gradually increased in size. On admission, the right testicle measured nine by six cm. It had retained its shape, was hard, and had a smooth surface. There was no pain. Testicular sensation was absent. The cord and inguinal glands were normal. January 14th, the right testicle was removed. A small hydrocele was opened into. Recovery uneventful. After-history: On October 1st, 1906, patient wrote that, since recovering his strength after the operation, he has had no illness whatever. He is in the best of health, and following his employment.

Macroscopic appearance.—There is a lowly-rising boss on the lower and outer part of the growth. On section the specimen is seen to be occupied by greyish succulent masses, the testicular substance being displaced to the periphery.

Microscopic appearance.—In the section preserved no derivatives of the *epiblast* are to be found.

Mesoblast.—The stroma is mainly fibrous. In places it is *myxomatous*, in others, *sarcomatous*. There are some collections of round cells resembling *lymphoid tissue*.

Hypoblast.—Numerous spaces and small cysts lined by *columnar cells*, with a central lumen. Some spaces are entirely filled by these cells, whereas they project into others in the form of papillary processes of connective tissue lined by two or three layers of cells. These cells are carcinomatous in appearance, no cells resembling those of adult mucous membrane being present.

Although we only find derivatives of the meso- and hypoblast, there can be no doubt that we are dealing with an *embryoma*. The appearance of the stroma and character of the epithelium exclude any other explanation of the nature of this growth. It

is a pity that this tumour is not available for re-examination. Although the section shows a distinctly malignant proliferation of the hypoblast, yet the patient was free from recurrence five years after operation.

CASE 58 (Museum No. 01⁴⁸).—R. F., 22, was admitted to Gloucester Infirmary for a tumour of the testicle which had been noticed for five months. It had been tapped six weeks before. On admission, the right testicle was enlarged and painful. The swelling extended up the cord. The tumour was removed.

Naked-eye appearance.—The testicle is twice its normal size. Except for several lowly-rising bosses it maintains its normal shape. On section it is honeycombed with cysts, which vary in size from half a centimetre in diameter to a pin's head. There is a small roughly triangular area in the anterior part of the growth which is free from cysts. The tunica vaginalis still surrounds the organ, and is intact, except below and behind, where the growth has fungated as a large, soft, irregular lobulated mass, with many bosses and processes, which almost completely fills up the cavity of the tunica vaginalis. When cut into, these masses present the same appearance as the primary growth. No traces of the original testicle can be made out.

Microscopic appearance.—I have examined sections removed from the greater part of the growth. In none of these have I been able to find any derivatives of the *epiblast*, although I have examined them all with a mechanical stage. The sections are practically a mass of cysts, among which narrow trabeculae of *mesoblastic* connective tissue run. The tissue is in places fibrous, in others more cellular, and in many very loose and myxomatous. Some cysts which contain no epithelium are surrounded by a thick condensed layer of fibrous tissue. There are bundles of *plain muscle* fibre and several *lymphoid follicles*, but I have been unable to find any cartilage.

Hypoblast.—The cysts are of all sizes; they occasionally bulge into each other. The majority of them are lined by *columnar epithelium*. In places this is tall, with many goblet cells, and oval nuclei; in others, and these are not necessarily large cysts in which the pressure may be supposed to have been great, the epithelium is shorter and the nuclei round, staining more deeply. In these cysts the cells may be arranged in several layers, but their characters are still those of hypoblastic and not of epiblastic cells. Numerous branching papillary processes project into these cysts. Many of the cysts contain what appears to be secretion, which may be homogeneous or more shreddy. Where the pressure has been great, the cells become cubical, flattened, and eventually disappear entirely. *Gland acini* lined by columnar epithelium lie scattered in the stroma. Many of these are distended by a hyaline secretion, which has produced flattening of the cells. The small triangular area which was described in the naked-eye examination of this tumour, as lying in front and being free from cysts, under the microscope reveals itself to be the remains of the *testicular substance*. The stroma between the tubules retains its loose character, and the tunica propria is never thickened. The intestinal cells of Leydig do not appear to be increased in number. In the immediate vicinity of cysts of new formation the seminal tubules are flattened, being reduced to narrow chinks, in which a few

epithelial cells can be seen. In the region removed from the growth the tubules appear of a healthy shape and size. Several layers of epithelial cells can be seen in their lumen. These cells appear to be healthy, but I have not seen any spermatozoa. Among these tubules there are some which are lined by only one layer of cubical epithelium, leaving a large lumen. Sections from the mass behind the testicle show the identical structures already described, with the exception, of course, of testicular substance.

In this specimen the hypoblast has grown at the expense of the other layers, reducing the mesoblast to a minimum amount of tissue around the cysts, and apparently having destroyed the epiblast.

CASE 59 (Museum No. 05²¹).—Robert McK., 58, was admitted to the General Hospital, Northampton, on April 8th, 1905, for a tumour of the right testicle, which he had noticed for five years. Growth had been slow until six weeks before admission, when it became rapid. The tumour was about the size of a hen's egg, hard, nodular, and painless. The upper part was softer than the lower. Testicular sensation was absent. No thickening of cord. No evidence of glandular enlargement. Castration. A small hydrocele was present. The tumour was sent to the Guy's Museum. The specimen is about the size of a tangerine orange. The tunica vaginalis is not adherent, and the epididymis is healthy. At the lower part of the testis there is a triangular, bony, new growth, with an irregular surface. Above it is the testicle.

Histological appearance:—

Epiblast.—No derivations of this layer appear in the section examined by me. In a report of the Clinical Research Association which is appended to the specimen, and who examined another piece of the growth, mention is made of cysts lined by *stratified epithelium*, and of areas of delicate granular tissue and cells resembling *grey nerve substance*.

Mesoblast.—The stroma is firm and fibrous. There are many thick-walled *blood vessels* and numerous small cysts. There are nodules of *lymphoid tissue*. Numerous pieces of *hyaline cartilage* are scattered about the section. The cells of this cartilage are small and comparatively few. Some of the cartilaginous nodules are surrounded by a thin layer of condensed stroma forming a *perichondrium* around them; others are surrounded by stroma which is more delicate and myxomatous in appearance, and the cells of which can be seen to become surrounded by the hyaline matrix to form cartilage. The former of these nodules may therefore be considered to be fully developed, whereas the latter are still growing. This cartilage in places is converted into *true bone*. Here the cartilage cells are arranged in rows, the spaces around them enlarge and coalesce to form spaces, in which can be seen cells and delicate connective tissue with capillary blood vessels. In other places, again, the bone can be seen in the process of being eaten away by a layer of large cells, or *osteoclasts*. At two or three spots the bone

appears to be formed directly from the connective tissue. We thus have *cartilage bone* and *membrane bone*. The Clinical Research Association found *unstriated muscle* in their section, but there is none in mine.

Hypoblast.—Cysts lined with tall *columnar epithelium*, which in some is ciliated, whereas in others *villi* are produced by the folding of the epithelium over connective tissue processes. There are also a few *tubular gland acini*. A large part of the section is composed of a diffuse infiltration with lines of epithelial cells, which are spheroidal in type, and are clearly a *carcinomatous* formation. One seminal tubule, represented by a hyaline mass, was seen in the middle of the new growth.

Here, again, we find derivatives of all the embryonic layers, one of which, the hypoblast, has taken on active malignant properties. This tumour had existed for five years, and we accordingly find large pieces of bone in it. For six weeks it had been growing rapidly, and we may assume that it then changed from a non-malignant into a malignant tumour.

Unfortunately, I do not know the after-history of this man.

CASE 60 (Kanthack and Pigg. Trans. Path. Soc. xlviii., p. 150.—“Malignant enchondroma of the testis; re-examination of Sir James Paget’s case, described in the ‘Transactions’ of the Royal Medical and Chirurgical Society, 1855, vol. xxxviii., p. 247.”).

Sir James Paget called this tumour a pure enchondroma, and it was mainly on his authority that it was believed for many years that an enchondroma may be malignant. He also thought that it had invaded the lymphatics, whereas it really had spread by the veins.

Mr. Strangeways has kindly allowed me to re-examine the sections that he cut for his paper in conjunction with the late Dr. Kanthack. I have published it here, since it is a classical case, and has, perhaps, been oftener quoted than any other specimen of malignant disease of the testicle.

The history is briefly as follows:—The patient was 37 years old. He had had repeated contusions of the testicle. The growth spread rapidly up the inguinal ring and was removed. Shortly after patient died of lung trouble. The right testis was almost completely replaced by a cartilaginous new growth. A thin layer of testicular substance was spread out over it. Above this a series of nodules of cystic new growth extended along the spermatic cord and were joined by a series of thickened vessels. The larger nodules contained cartilage. The thickened right spermatic vein could be traced into the

inferior vena cava. At the junction of these vessels there was a large cystic mass with pieces of cartilage. Three small cartilaginous tumours were found within the cava, and numerous cartilaginous nodules in the lungs, and small filamentous growths in the larger branches of the pulmonary arteries. The growth had evidently disseminated by the veins. The lymphatics were free.

Microscopic examination.—*Testis.*—Slides from two parts of the growth have been examined.

The first is from the centre. In it there are no *epiblastic elements*. The *mesoblastic* tissue predominates; there is a delicate *myxomatous tissue*, in which there lie large masses of *hyaline cartilage* of oval and irregular shape, surrounded by a perichondrium. The cells in the middle of the cartilaginous nodules are much larger than those at the periphery. These nodules are so abundant that the connective tissue is reduced to a network of delicate processes lying between them.

Hypoblast.—In the stroma a few small spaces filled with the remains of columnar and spheroidal cells can be seen.

The *second section* again shows no *epiblastic tissue*. The mesoblast consists of a much more abundant *connective tissue*, which in places is *myxomatous*; there are large masses of *cartilage* resembling those already described. Groups of cysts are to be seen, around which the stroma is more condensed; it sends papillary processes into the lumen of some of them. The epithelium lining these cysts is hypoblastic, consisting of tall *columnar* or of *spheroidal* irregular cells. There are also a few tubules resembling *gland alveoli*. Two of the masses along the *spermatic cord*, which were removed during life have been examined. Here *epiblastic* structures in the shape of *epithelial pearls* are visible. In other respects these masses resemble the testicular growth, except that the connective tissue is more abundant and more cellular. A section taken right across the *spermatic vessels* within the abdomen shows the artery to be unaffected. The growth lies in the veins, as has been shown by Kanthack and Pigg. No *epiblastic structures* are visible. There is a *mesoblastic* connective tissue with several nodules of growing *cartilage*, since the change from stroma to cartilage can be observed; and numerous cystic spaces, lined by *columnar epithelium*.

Growth in front of vena cava.—Here we have well-marked *epiblastic* structures, consisting of large areas of *stratified squamous epithelium*, in the more central parts of which the cells have become cornified so as to form very large *epithelial pearls*. Some of these are as large as those seen in an epithelioma of the skin, but the cells show no tendency to infiltrate the stroma. There is a *mesoblastic* fibrous stroma with *cartilage*, and *hypoblastic* columnar epithelium forming the lining of numerous cysts and spaces.

Growth within vena cava.—*Epiblast* not represented. Other two layers present in form described above. The cartilage is very abundant.

Growth from lung.—Here again the *epiblast* is not represented.

Mesoblast.—Cartilage is very abundant.

Hypoblast.—Numerous spaces lined by columnar epithelium, and one large cyst, with papillary processes formed by the stroma. On these the epithelium, which is very tall and contains many *goblet cells*, is arranged in the manner characteristic of *intestinal villi*.

In this tumour, or in its metastases, derivatives of all the embryonic layers are to be seen. The most striking feature of the case is the entirely non-malignant structure of both primary and secondary tumours. Although there are deposits in the lungs, yet they contain nothing but fully differentiated structures. It is very unfortunate that no metastases from any other of these cases were available for examination. Whereas the tumour now under consideration spread by the blood-stream, it did so *en masse*, structures being present in the metastases that are not observed in the primary growth. It is safe to say that if the metastases of a case such as case 39 had been examined, they would have been found to consist entirely of a columnar-celled carcinoma, and to be glandular in their spread. In case 40 the spread was by the lymphatics, but, unfortunately, no pieces were preserved.

We therefore learn from this case that, although an embryoma may show no malignant changes, yet it may disseminate by the blood stream. No doubt, the primary tumour had burst into one of the spermatic veins, and small pieces were carried away by the blood-stream to distant parts, where they found a suitable soil for growth.

CASE 61 (Surg. Reg. No. 1976 (2002). Surg. Rep., 1904, Symonds, 576).—Catherine C., 49, was admitted on September 11th, 1904, for a strangulated left inguinal hernia. Patient is married, but has had no pregnancies. She has never menstruated. Her sexual desires have always been for women and not for men. During the operation for relief of the strangulated hernia, a small body, which was of the size of the ovary and mistaken for it, was found in the hernial sac and removed (No. 1976). As patient showed signs of intestinal obstruction, laparotomy was performed on October 5th. A loop of intestine was found, which showed evidence of having been strangulated. In its mesentery two small nodules of growth (No. 2002) were found. The loop of intestine and its mesentery were resected. Patient made a good recovery, and left the hospital on November 9th. She was examined by the gynaecologists, who reported that no uterus could be felt, the vagina ending blindly two inches up. There was no cervix.

Naked-eye appearance.—The tumour removed was about an inch long and half an inch broad. On cutting into it, it was found to be of a fibrous consistency, surrounded by a thick capsule. In the fibrous growth two fairly large nodules of a darker colour were seen; these nodules were circumscribed. A few similar minute points could be seen scattered about. The tumour was attached by a pedicle, consisting of fibrous tissue and blood vessels.

Microscopic examination.—I was able to cut sections across the whole surface of the growth. The capsule consists of dense fibrous tissue, containing at the hilum many blood vessels and some plain muscle. The stroma of

the growth is made up of looser fibrous tissue, which contains many blood vessels, and lying scattered about in it a few acini, which closely resemble degenerated testicular tubules, each being surrounded by a tunica propria. These acini are few in number, there being not more than a dozen in the whole section. Also, scattered about in the stroma, there are numerous cells which correspond with those presently to be described in the nodules, and which I therefore believe to be *interstitial cells* of Leydig. They tend to occur in groups of twos and threes.

The *smaller of the two big nodules* is shown to be surrounded by a capsule formed of condensed connective tissue and continuous with the stroma. It is made up of a mass of closely-packed testicular tubules. In some places these tubules are so closely packed that they assume a roughly hexagonal form from mutual pressure; in other places they are farther apart. Each tubule is surrounded by a thin homogeneous *membrana propria*, without nuclei, and where they are most numerous they are separated merely by these membranes. In other places there is a certain amount of connective tissue, which is, however, denser than that of a normal testicle. Everywhere among the fusiform nuclei of the connective tissue there are large rounded cells with a homogeneous protoplasm, which stains rather deeply with eosin, and, in places, shows signs of a fatty change; their nuclei are rounded, and many of them contain one or more distinct nucleoli. I have compared them with the interstitial cells of Leydig in a section of a testicle, and they are identical with them in appearance. In places these cells are so closely packed and numerous as to completely fill up the spaces between the testicular tubules, to the exclusion of the connective tissue cells. The epithelium of the tubules consists of several layers; it shows no signs of degeneration. Indeed, it resembles the testicle before puberty.

The *larger nodule* is also encapsuled. At its periphery it consists of the same tissue, only the intestinal cells are even more abundant. As we near the centre, without any sharp line of demarcation, the connective tissue becomes more abundant, and forms small alveoli, which are directly lined, without the intervention of a *membrana propria*, by one or more layers of cubical epithelium, with a central lumen. In some spaces the cubical cells entirely fill up the lumen, whereas in others it is occupied by a more or less round body with a clear-cut outline, which is homogeneous and has stained deeply with eosin. These bodies resemble the "*corpora amylacea*" of the prostate, and, indeed, the whole of this tissue so clearly resembles that gland that it must be called prostatic tissue. This statement has been confirmed by Mr. Targett. There is, however, no plain muscle, and the interstitial cells of Leydig can be seen in some numbers in its stroma. This prostatic tissue, in one or two places, comes to the surface of the nodule.

The *smaller nodules*: One of these is made up of prostatic tissue with *corpora amylacea*. The others consist of what I, at first, considered to be suprarenal tissue. On closer examination, however, I believe that they are masses of interstitial cells. They are identical in appearance with those found in the larger nodules. Although in some places they are tightly wedged together, in others they are not so numerous, and here they can be seen lying between the connective tissue cells. Although there are numerous capillaries present, these are not arranged around masses of cells in the manner characteristic of the suprarenal body. These masses are very

numerous, and some are large enough to be seen by the naked eye. Although the majority are circumscribed, they have no definite capsules, and some can be seen spreading into the surrounding stroma.

The *nodules from the mesentery* consist merely of inflammatory material.

On considering the features of this case, I think there can be little doubt that this person is really a male. The history of absence of menstruation and of perverted sexual desires point to this conclusion. It is also supported by the absence of a uterus. If we take this person to be really a male, it throws some light on the structure removed at the first operation. The presence of testicular tubules and of interstitial cells in its stroma seem to indicate that the organ is a testicle. It may therefore be taken to be a testicle in which the seminal tubules have undergone a very great degree of atrophy, only a few remaining. The connective tissue has hypertrophied to a corresponding extent, and Leydig's cells have increased in number, this increase taking place to a great extent in several localised areas. In this atrophied testicle a growth has been formed containing testicular and spermatic structure. Two explanations of this appearance may be offered. One is that we are dealing with some error of development. The external generative organs were shown to be mal-developed. Then why not the internal? The great difficulty to the acceptance of this theory lies in the fact that the testicle is developed high up, and the prostate low down in the body. But it is not impossible that the testicle may early have been dragged down into the pelvis, have come in contact with the developing prostate, and have included within it a portion of this gland.

The other explanation is that we are dealing with a tumour of the testicle analogous to an embryoma, in which testicular and prostatic tissue has developed to the exclusion of the other tissues of which it was originally composed. I have described in case 55 a well-formed mucous gland. Its structure is as perfect as that of the testicular and prostatic tissues in the present specimen. If the one occurred in an embryoma, there is no reason why the others should not. The only difference lies in the fact that in this case all traces of the other tissues of the embryoma have disappeared.

CONCLUSIONS.

It will be necessary to review shortly the various tissues which have been found in the present series of cases. I have already attempted to divide them into structures derived from the three primary embryonic layers, a classification which is warranted by their appearance, and will now enumerate them in order:—

i. *Epiblastic structures*.—Here we find stratified epithelium forming a lining for cysts, or running in the stroma in the form of solid epithelial rods. This epithelium closely resembles that found on the skin, the different layers of which it is composed being in many places evident. The external layer is often columnar, resembling the rete Malpighii of the skin. The deeper cells become larger and clearer. Eventually the central cells undergo a horny change, producing the epithelial pearls which can be seen in the healthy skin, in inflamed areas, and in epitheliomata. In one case (49) the epithelium is transitional in type, resembling that of the bladder. Other structures derived from the epiblast are a tooth (47); grey nerve matter, as observed by the Clinical Research Association in case 59; a spinal ganglion (43); a rudimentary retina (45); a spinal cord (46). In case 60 no epiblastic derivative was found in the primary growth, although present in some of the metastases. In cases 44, 48, 52, 57 and 58 no epiblastic structures were found.

ii. *Mesoblastic structures*.—The stroma consists of young connective tissue, which closely resembles that of the embryo. In some cases it is fibrous, in others it is more cellular, resembling a round or spindle-celled sarcoma. Myxomatous change is often present. Most of the cases show pieces of hyaline cartilage, which in two instances (48 and 60) was developed to an enormous extent. Bone occurs once (59). Unstriated muscle is frequently present; striped muscle on two occasions (43 and 44). Lymphoid follicles are common. In one case (47) giant cells are formed, whose function seems to be to destroy and erode the dead epithelial pearls.

iii. *Hypoblastic structures*.—Columnar epithelium with goblet cells, resembling the epithelium of the intestinal mucous membrane, is present in many cases as a lining to the cysts. This resemblance is often increased by the presence of villi and of longitudinal and circular bands of unstripped muscle around the cysts. Ciliated columnar epithelium resembling that of the respiratory tract is almost equally common. It is most fully developed in case 55. In many cysts the epithelium is cubical or flattened from pressure. On the other hand, there may be several layers. Many cysts contain a secretion which has been formed by the cells. In different cases it stains differently, which is probably due to different chemical composition. When goblet cells are abundant the secretion consists chiefly of mucin. Besides the lining of cysts, there are present many alveoli lined by cubical or columnar epithelium, resembling tubular glands. There are also numerous areas in which the columnar or cubical cells have infiltrated the connective tissue, producing an appearance of columnar or spheroidal-celled carcinoma.

Usually the hypoblast is in excess of the epiblast. In two cases (45 and 53) it is wanting.

We see, then, that in most of these cases structures are present which arise from the three primary layers of the embryo.

With regard to the site of origin of these tumours, it can be shown in every case that they originate within the testicle, since the tunica albuginea can be traced around the tumour. In many cases a thin layer of testicular substance can also be seen to be spread out over the periphery of the new growth. This seems to indicate that the growth begins in the back part of the testicle, in the neighbourhood of the rete testis, since in no case, which I have been able personally to examine, can any testicular substance be found behind the growth. In many cases the epididymis lies flattened, but otherwise unchanged, behind the growth; in others it is involved within it. In no case can the tumour be shown to have originated in the epididymis.

On section these tumours present a varying appearance ; some are composed of little else than a mass of cysts, with a minimal amount of connective tissue between them ; others, again, present a solid, homogeneous appearance, with but a few almost microscopical cysts. In two cases (41 and 59) the tumour was circumscribed and encapsuled. This capsule is formed by its expansive growth producing a certain degree of inflammation in the surrounding tissues with subsequent fibrosis.

I have enumerated above the various histological structures which I have found. It is interesting to note, if we leave out of consideration case 61, that the structures are nearly always of a simple kind. If we examine the epiblastic structures, we see that the skin is merely represented by epithelium, there are no hairs, sebaceous or sweat glands, or papillæ. An exception to this is the developing tooth. This is, however, still in a very embryonic form. The mesoblast is, as a rule, richly cellular, but shows the formation of differentiated tissue, such as muscle, cartilage, and in one case bone, to a much greater extent than the epiblast. The same applies to the hypoblast, in which the epithelium is often arranged in the shape of villi, and is surrounded by a circular and longitudinal layer of plain muscle.

Of these three layers the one which is least in evidence is the epiblast. Only twice (45 and 50) is it in excess of the hypoblast. When a layer is missing it is also most frequently the epiblast. This seems to show that it is least developed, owing to the conditions being less favourable to its growth than to that of the other layers. In dermoids, however, the epiblastic structures are always in excess. This difference may be due to the difference in tension which is set up in the two cases by the surroundings. The epiblast is normally a structure which covers the external surface of the body. The conditions for its growth, therefore, more closely approach the normal in the large cavity of the dermoid.

The absence of one layer may be accounted for by supposing that, at the beginning of the growth of the tumour, the cells which were going to form it have been overgrown and destroyed by the stronger growth of the other two layers. As I have said,

it is usually the epiblast that is missing, which is the layer which has the greatest difficulty in growing. Wilms describes an ovarian dermoid in which the hypoblast was missing. In a dermoid we may suppose that the open nature of its structure is not so favourable for the growth of this layer as it is for that of the epiblast.

Another explanation is suggested by case 47, in which the cell perls were being eroded by connective tissue giant cells. If this process should go on to a marked extent, the whole of one layer might disappear. I believe, however, that the giant cells will merely attack the dead tissues, which act as foreign bodies.

The third explanation, which is probably the correct one in most cases, is that the layer in question is present to such a limited extent that it has been overlooked.

The cysts and spaces have been shown by injection experiments to intercommunicate with each other. This leads one to suppose that the growth has taken place along præ-formed channels. Wilms has demonstrated that these channels are the testicular tubules by showing how, in places, the cells of the new growth can be seen to run within their interior. This statement is not borne out by the cases just described, in most of which growth seems to have taken place along the lymphatic channels. The cysts have arisen from local excessive growth of the epithelium of the tumour, which has blocked up the lumen of the tube.

The cysts are nearly always lined by one kind of epithelium only. In two cases (41, 46) there are present cysts lined by stratified and columnar epithelium. As has been pointed out when describing the cases, there is, however, no sign of the two kinds of epithelium merging into each other, the line of junction between them is always perfectly sharp. There is, therefore, no metaplasia, or change of one form of epithelium into the other. The appearance can be explained quite satisfactorily by assuming that the epiblast and hypoblast have invaded the same space during the growth of the tumour, and that they are now found growing in it side by side.

When the mesoblast is in excess, the tumour is compact; when the other two layers, it is cystic.

The structures of all the layers may undergo a malignant change. When it is the mesoblast that does this, we get an appearance of sarcoma; when the hypoblast, there is an appearance of spheroidal or columnar-celled carcinoma. When discussing the chorion-epitheliomata, it will be shown that the epiblast is also capable of undergoing this change.

Not only may one layer be greatly in excess of the others, but one tissue may assume this supremacy. Case 43, which consists almost entirely of striped muscle, illustrates this point well.

To distinguish these tumours from dermoids, they are often called solid embryomata, whereas dermoids are known as cystic embryomata.

It is now necessary to say a few words about dermoids of the testicle. They are far more uncommon than the class of embryomata that have hitherto been discussed. There is no specimen preserved in the museum. Wilms gave a very excellent account of these in 1896. He shows that there is much confusion in the classification of these cysts, many cases being reported as dermoids of the testicle which were situated outside the tunica albuginea, whereas only such cysts as lie within the albuginea have originated within the testicle. These testicular dermoids all show a complicated structure, they possess a process or "Zotte" projecting into their interior. This Zotte is composed of the three germinal layers and contains a great deal of nervous tissue, and corresponds to the anterior end of the embryo. The epiblastic structures, which are always in excess, show a well-developed cutis with all of its appendages. The chief point which distinguishes these "cystic" from the "solid" embryomata is the comparatively high degree of development which their structures have attained.

Ovarian dermoids resemble these testicular dermoids in all essential details, and can always be shown to contain a well-formed anterior extremity of the embryo. They may be multiple. One tissue may be developed to the exclusion of all others in a very marked degree. In some cases this is the thyroid. Bell, Pick, and Walthard have collected several such cases, in which the patient did not suffer from thyroid disease. Ovarian dermoids are far commoner than ovarian "solid" embryomata, which latter

resemble those of the testicle in their main features, but their structures are rather more developed, hairs and the other cutaneous appendages being often found. They also resemble dermoids in that the anterior end of the embryo can be shown to be better developed than the posterior end. They are occasionally found in company with a dermoid.

There is, therefore, no fundamental distinction between dermoids, or cystic embryomata, and the solid embryomata. The main differences between them seem to lie in their mode of growth and the pressure which the tissues in which they originate exert upon them. This also explains the rarity of cystic and the frequency of solid embryomata in the testicle, and the inverse degree of frequency of these two forms in the ovary.

We may classify these tumours according to the complexity exhibited by their structures, taking the least complex first.

- (1.) Testicular solid embryomata.
- (2.) Ovarian solid embryomata.
- (3.) Cystic embryomata or dermoids.

Ætiology and Development.—The mere fact that such a large variety of new growths have been described as occurring in the testicle which are not found anywhere else, shows that their pathology has not been understood. Among others, the following names have been applied to them: chondro-sarcoma, chondro-carcinoma, both simple and cystic; myo-sarcoma; myo-chondro-sarcoma; cystic disease, etc., etc. I have attempted to show that all these tumours are essentially the same. This confusion of names implies a corresponding confusion in the authors' ideas of their development. Some of the views which have been held as to the origin of these tumours are as follows:—

An early view was that these tumours originate in the epithelium of the seminal tubules. Its cells were supposed partly to produce the epithelial elements of the new growth, and partly to give rise to the connective tissue and cartilage. This view is untenable, for it presupposes that epithelial cells are able to undergo a change into connective tissue cells. But it is quite impossible for a cell which has become fully differentiated into epithelium to undergo any such change. It is even impossible

for epiblastic epithelium to become converted into hypoblastic. A cell can only change into another when both have developed from the same mother cell. An example of this is the occasional appearance of stratified epithelium in parotid tumours. The parotid is developed from the epiblast of the embryonic mouth. Its cells go, some to form the stratified epithelium of the mouth, others the columnar epithelium of the salivary glands and ducts. It is quite possible, therefore, that under special conditions the columnar epithelium of the salivary ducts may become converted into stratified epithelium, of which it may be considered to be merely a variety. It is quite impossible, however, for the differentiated epithelium of the seminal tubules to be converted into connective tissue or even stratified epithelium. This is the view that Foulerton has recently attempted to uphold. Another view is the one put forward by Shattock for cystic disease of the kidneys, and extended by Bland Sutton to this class of tumour of the testicle. It tries to prove that these tumours originate in remains of the Wolffian body. Bland Sutton thought that these remains were the organ of Giraldes. Eve, however, pointed out that these tumours originate between the testis and epididymis, and derived them from Wolffian remains in this situation. This theory does not explain any more than the former why there should be stratified epithelium and cartilage in these tumours.

Bushnell has recently described a tumour which showed areas resembling a carcinoma, sarcoma, and endothelioma. He himself did not regard this case as an embryoma, although his diagnosis is, I think, open to doubt. He traces its origin from the tubuli recti, and explains its complicated appearance as arising from the potentialities of growth of the "mesothelium" of the rete testis. This sounds pretty, but explains nothing.

A third explanation is that of foetal inclusion. According to this view a rudimentary foetus has been included in the body of the patient, and lives a parasitic existence on his tissues. This may explain similar tumours found in the middle line and in the cavities of the body, but not testicular embryomata, which are always developed beneath the tunica albuginea, and therefore in

an organ which did not open into the peritoneal cavity at a time when the parasitic fœtus may be supposed to have been included.

Wilms, in 1896, was the first to suggest that the embryomata of the reproductive glands originate in the reproductive cells. In the ovary these are the ova, in the testicle the spermatozoa. This development is, therefore, analogous to a process of parthenogenesis, for which, however, there is no evidence in the higher animals. Bonnett and Marchand derive the embryomata from isolated blastomeres, cells which at an early developmental period have become isolated from the general growth of the individual, and, after lying dormant, have taken on an independent growth. There is evidence to show that a complete fœtus may originate from the cells of the first or even the second division of the ovum. These authors have also suggested the possibility of these tumours originating in polar bodies which have not perished. But it is a fact, which it is difficult to explain on the lines of Marchand and Bonnett, that this class of tumour occurs almost exclusively in the reproductive glands. It is incomprehensible why the blastomeres, or polar bodies, should wander to these comparatively small organs in nearly every case. While we may assume their origin from these bodies in the embryomata, which are occasionally found in other parts of the body, it seems necessary to regard the majority of those that have arisen in the reproductive glands as being derived from the sexual cells. Although the fully-formed reproductive cells can never give rise to a parthogenetic formation, it is not impossible that the cells from which they are derived, the "Ureier," may do so to a limited degree under abnormal conditions. Weismann considers that the nucleus of the ovum contains two kinds of protoplasm, the "germinal," which is derived unchanged from the parent ovum, and produces the impulses whereby it is able to grow into a new individual; and the "histogenous," which is derived from the germinal, dominates the ovum during its development and ripening, and is extruded when the ovum is matured, so as to enable the germinal protoplasm to gain the upper hand. As long as the histogenous protoplasm preponderates there is no attempt

at division. It is possible that this kind of protoplasm may, under certain pathological conditions, disappear or become dormant. The germinal protoplasm then assumes the upper hand, and the cell divides and forms an embryoma. Whichever of these views may turn out eventually to be the correct one, there can be no doubt that these tumours which contain derivatives of the three blastodermic layers must have originated in a cell which is analogous to an ovum (including a spermatozoon) or one of its earliest divisions, *i.e.*, a cell which is still capable of producing the three primary layers of the embryo. The development of an embryoma proceeds on the same lines as does that of an embryo, and there is nothing more incomprehensible in the one than there is in the other. We need no longer call such obscure and doubtful processes as metaplasia to our assistance.

This view also throws some light on the origin of many malignant new growths. If they arise in cells which ought to have developed into the structures of the fully-formed part, but have failed to do so and have remained dormant, there is no difficulty in explaining the rough resemblance these tumours bear to the tissue or organ from which they spring.

Taking, then, the fact for granted, that embryomata of the sexual glands arise in the reproductive cells, an explanation is at once found why dermoids are so common in the ovary and rare in the testicle, and why the solid embryomata behave in the reverse manner. When one of these tumours arises in the ovary, its seat of origin is the Graafian follicle. This forms a comparatively large cavity, in which the tumour is able to grow in a compact and more highly organised form than is possible in the testicle, the narrowness of whose tubes compels the growth to extend in an irregular manner. Conditions which enable the tumour to grow in a compact form as a dermoid must necessarily be very rare in the testicle.

I must mention that Petrow has recently produced an embryoma, experimentally, in the testicle of a guinea-pig, by injecting into it an emulsion of the tissues of very young fetal guinea-pigs in normal salt solution.

History.—The average age of sixteen patients at the time of operation is 29. The youngest was 1 year and 10 months, the oldest 58. The average duration before operation is five and a half years. Two cases were congenital, one being 2 and the other 29 years old. The longest history is seventeen years and the shortest one month. After-history:—One patient was killed ten years later; one is alive six years later; three died within a year of the operation. I have been unable to ascertain the after-history of the others. This history is good, since the patients that died did so very soon after the operation. No doubt many of those who were lost sight of are still alive.

Metastases and Malignancy.—The tumours are able to disseminate in two ways. Either the metastases are composed of all the tissues of the primary growth, which need not have undergone any malignant change, or one tissue has become actively malignant and disseminates.

(a.) Let us examine the first possibility. In case 60 the growth had pierced the spermatic veins, and deposits were found in the vena cava, pulmonary arteries and lungs, the lymphatics being free.

The striking feature of this case is the great tendency for the new growth to eat its way into the vessels and to form solid cords in them. Malignancy would seem here to be due to a piece of the tissue having got into the vessels and being carried away by the blood-stream. Individual cells do not seem to have done so in the same way as happens in a sarcoma or a carcinoma, for then we should expect to find each metastasis to consist of only one form of epithelium or connective tissue. For we can scarcely assume that among the cells of the embryoma, which all show a good degree of differentiation, some which are analogous to reproductive cells should remain, which can give rise on their own initiative to the three embryonic layers.

(b.) One tissue may have undergone a malignant change. Unfortunately there is no microscopical examination of the metastases of such a case. Hicks and Targett, in a paper on embryoma of the ovary, mention that the secondary growths often show the structure of a round-celled sarcoma. In case 39,

in which an iliac gland was felt to be enlarged, and in which the tumour recurred as a columnar-celled carcinoma, it is more than probable that the metastases, if examined, would have shown a similar structure. If the secondary deposits are sarcomatous, we would expect the tumour to spread by the blood-stream; if carcinomatous, by the lymphatics. I can, however, produce no evidence in support of this supposition.

CHORION-EPITHELIOMA.

This series of cases comprises four which show a formation of chorion-epithelioma. They are here considered under a separate heading, since they present distinct features of their own. It must be remembered, however, that they are merely embryomata, in which the ectoderm has assumed the characters of the trophoblast.

The following case was published by Mr. Reinhold in the *Guy's Hospital Gazette*, vol. xix., No. 453. A good account of it will be found in the *Lancet*, May 25th, 1906, p. 1471.

CASE 62.—Walter P., 30, was admitted into St. John's Hospital, Lewisham, in May, 1905, for an enlargement of the right testicle, which he had noticed for nine months. There was no pain or tenderness, only a dragging sensation. It increased markedly in size in December, 1904, and was punctured, but no fluid was withdrawn. On admission, the tumour was restricted to the testicle, which was of the size of a "William pear." The cord was not thickened. The left testicle was healthy. Patient was well three months after the operation.

Naked-eye appearance.—The growth is limited by the thickened tunica albuginea. The surface is smooth. On making a section through the tumour it is found to be made up of a tough fibrous matrix, in which there are several small cysts. In the centre there is a soft hæmorrhagic patch. The epididymis is invaded by the new growth.

Microscopical appearance.—The greater part of the tumour is so necrotic that it is impossible to make out any definite tissues. Two small pieces taken from near the central hæmorrhage, however, have not suffered, so that sufficient can be made out for purposes of identification. In an area which consists principally of extravasated and organising blood, large masses of tissue, identical in appearance with the embryonic trophoblast, can be seen. It consists of large collections of cells with no intercellular connective tissue. These cells in many places project into and even completely surround blood vessels and spaces, and are composed of two kinds of cells; (a) small cells, with a clear, non-staining protoplasm, and a relatively large vesicular lightly-staining nucleus. They are rounded or polyhedral from mutual pressure, and make up the bulk of the masses; these are *Langhans' cells*; (b) irregular,

dark staining masses of protoplasm with many nuclei, which are smaller as a rule than those of the discrete cells, although they may be very large, and stain a very deep colour. These *syncytial masses* are generally spread out as a thin layer over the surface of the *Langhans' cells*, especially where they project into the blood vessels. In other places they become thickened to form large masses resembling big multinuclear giant cells. They may also be seen occurring between the *Langhans' cells*. Some large spaces, filled with unaltered blood with many leucocytes are entirely surrounded by these two kinds of cells. In the organising blood large areas of leucocytic infiltration are visible.

In another part there is a large mass of new growth resembling a *carcinoma*, being in parts alveolar and in others papillary. There is very little connective tissue among these processes, only the largest papillæ containing a little in their interior. The epithelium consists of one or more layers of cells, columnar on the surface, becoming cubical and polygonal deeper down. The nuclei of these cells are vesicular and rather faintly staining. Among these cells can be seen some of an elongated or irregular shape, with one or more darkly-staining nuclei. Several cysts can be seen lined by tall *cylindrical* or by *cubical* epithelium; into some of these, papillæ of connective tissue with epithelial lining project. The stroma consist of a myxomatous connective tissue, in which there are many bundles of *unstripped muscle*, and some cross sections of *peripheral nerve*.

On examining this tumour we therefore find derivatives of the three blastodermic layers. From the *epiblast* are derived the nerve bundles, the chorion-epithelioma and the carcinomatous growth. This latter has been shown by Emmanuel to be produced from the *Langhans' cells* of the chorion-epithelioma, as I shall have occasion to mention more fully later on; the syncytium being represented by the few cells with the small deeply-staining nuclei. The *mesoblast* is represented by the connective tissue stroma, and the unstripped muscle. Of *hypoblastic* origin is the columnar and cubical epithelium lining the cysts. There can, therefore, be no doubt as to the embryomatous nature of this tumour.

CASE 63 (Museum No. 2119. Green Inspections, xiv., p. 15).—John S., 30, was admitted in June, 1828, for cough and hæmoptysis. He was very wasted. Death occurred a few days after admission. A large mass was found fungating from the upper part of both lungs and attached to the ribs. Both lungs contained many small nodules of growth. There was also a growth, two inches in circumference, in the right cerebral hemisphere. The right testicle was enlarged.

Naked-eye appearance.—The tumour is injected with some colouring agent. It is four and a half inches in length, and has many bossy prominences on its exterior. The cut surface presents fibrous trabeculae, separating dark

grey masses of new growth. There are numerous ragged cavities occupied by blood-clot and injection. Several dark hæmorrhagic areas stand out conspicuously.

Microscopic appearance.—The greater part of the section consists of organising blood-clot. Among this in several places are seen masses of Langhans' cells and of syncytium mixed up together. The appearance of these cells is the same as that of case 62. Some fibrous stroma containing a large amount of unstriped muscle can be seen in another part of the section.

Although derivatives of but two embryonic layers are to be made out, there can be no doubt as to the embryomatous nature of this tumour.

CASE 64.—Walter A., 20, was admitted on October 29th, 1906, into Addenbrooke's Hospital, under Mr. Deighton (who has kindly allowed me to make use of this case), for enlargement of the left testicle. He first noticed it in January, 1906, a few days after a wrestling match, when he received a knock. There has been no pain. On admission, patient is a fine-looking man. The tumour is uniform. The epididymis can be felt stretched out over the back of the tumour. The cord is not thickened. No signs of metastasis. The tumour was removed. There was no hydrocele. Patient was discharged with the wound healed by primary union. December 20th. Patient has a large abdominal recurrence.

Naked-eye appearance.—The tumour measured three and a quarter inches in length and two and a quarter inches antero-posteriorly. Its external surface is smooth. The two layers of the tunica vaginalis are thickened and are partially adherent to each other. The epididymis can be made out. The cut surface of the tumour, which was opened in the antero-posterior direction, shows under a thickened tunica albuginea an infiltration with new growth. No remains of the testicular substance can be made out. The new growth consists of an upper and lower roughly triangular area, which is composed of white fibrous tissue in which there are a few cysts. The remainder of the surface is made up of a large hæmorrhagic shreddy mass, in which the remains of necrotic trabeculae and a few cysts are seen. The hæmorrhages in some places seem to be much more recent than in others.

Microscopic appearance.—I have examined sections taken from many parts of the growth. Nearly all of them consist of organising blood-clot and large necrotic areas in which the structure of the tissues has been entirely lost. Sections prepared from the white areas and from a few other places, however, still show the original tissues in a sufficiently good state of preservation.

Epiblast.—There is a cyst lined by stratified epithelium and another occupied entirely by a large cell-perl, in the white areas of the growth. In the hæmorrhagic portion numerous areas of syncytium and of Langhans' cells can be seen in an excellent state of preservation, the dark masses of the former contrasting well with the light well-defined cells of the latter.

Mesoblast.—The stroma is very firm and fibrous and contains everywhere large bundles of unstriped muscle fibres. There are localised areas in which it has undergone mucoid softening. I have seen one small nodule of hyaline cartilage.

Hypoblast.—There are cysts lined with tall columnar epithelium. In others, which are distended with secretion, the epithelium has become cubical or flattened. Alveoli, filled with spheroidal cells, are sparsely scattered about in the stroma.

Here, again, derivatives of the three blastodermic layers can be demonstrated.

CASE 65 (Curator's room, No. 98⁹⁰. Insp., 1898, 161).—Walter W., 25, was admitted in April, 1898, for pains in the abdomen and loins, which had troubled him at intervals for the last two years. Three weeks before admission he began to lose weight and appetite. Since then he has had slight difficulty in micturition. No history of gonorrhœa. On admission, the left testicle was much larger than the right. Just below the left costal margin there was a tumour, over which the skin moved freely. Patient's weight was 7st 11lbs. The tumour increased in size, the abdominal pain became worse, and persistent vomiting and constipation set in. Patient's weight fell to 7st 5lbs in three weeks, and he had a slight attack of hæmatemesis (*sic*). A laparotomy was performed, but the abdominal growth, which appeared to be located in the head of the pancreas, was found to be inoperable. Patient sank rapidly with dyspnoea and signs in the lungs.

Post-mortem inspection.—In the abdomen a large dark mass was found to the left of the middle line, lying beneath the stomach and partly under the pancreas, which latter organ was healthy. It was composed of malignant deposit with a large blood-cyst in its centre. The aortic glands on both sides were enlarged by new growth. Both lungs were filled with secondary deposits, which were hæmorrhagic and softening. The bronchial glands were not involved. The liver was large; it weighed 79ozs., was nodular on the surface and full of masses of growth. The left testicle was enlarged.

Naked-eye appearance.—The testicle is twice the normal size. It is entirely occupied by a faintly lobulated new growth which is yellow and necrotic in the centre, and at the periphery shows several areas of hæmorrhage. The epididymis and vas are healthy. A slice of the liver is preserved which shows numerous round nodular masses of growth, the largest of which are two inches in diameter. They present a very hæmorrhagic appearance.

Microscopical appearance.—I will describe the nodules in the liver first. These show a great deal of extravasated blood. Projecting into this everywhere can be seen large masses of syncytium and of Langhans' cells. The former is the more abundant and is arranged in the shape of irregular villous growths, long thin bands, or large multinucleated protoplasmic masses. The protoplasm stains deeply, and the nuclei, of which in places there are many, are dark. There are many vacuoles, some of which contain red blood corpuscles and even leucocytes. The Langhans' cells are arranged as groups of small cells with definite cell outlines and large clear vesicular nuclei in the midst of the syncytium. I may add that this specimen has been taken by several persons to be a metastasis of an uterine chorion-epithelioma,

The primary growth presents a totally different appearance. The stroma is everywhere firm and well formed. It forms a very wide meshwork enclosing large spaces. The spaces are filled with cells which present a

papillary, alveolar, or circumvascular arrangement resembling a columnar-celled carcinoma or an endothelioma. There are some areas which are more definitely sarcomatous in appearance. There is very little connective tissue in these areas. The cells themselves are uniform in size, with a very lightly-staining protoplasm, and a large, clear, vesicular nucleus, with distinct nucleolus. They resemble very closely the Langhans' cells of the metastases in the liver. I consider them in reality to be Langhans' cells, which have undergone the change in appearance I have already described in case 62. Among them a few small deeply-staining nuclei can be seen, which represent the remains of the syncytium. The resemblance to Langhans' cells is most marked in an area in which there is a large clump of cells. Here I have seen a small protoplasmic band with several nuclei. There is another part of the section in which the stroma is firm and abundant and encloses small spaces and narrow clefts which are lined by one or more layers of cubical cells with clear nuclei. These cells are, however, much smaller and take the stain more deeply than the cells described, and their nuclei are smaller. This area of the growth resembles very closely an endothelioma.

In this growth there are present only derivatives of the ectoderm and mesoderm. The true nature of the tumour is obscured in the primary growth, which might easily be mistaken for an endothelioma. It is not until we examine the metastases that the true embryomatous nature of the growth is revealed.

CONCLUSIONS.

It will be seen from the description of cases 62-65 that they are all embryomata of the testicle, in which there is a formation of trophoblast, so that fields of the section closely resemble a chorion-epithelioma. This trophoblast, which originates from the epiblast of the tumour, has assumed an active growth and reappears in the metastases.

I will shortly enumerate the tissues that have been found in these four cases:—

i. *Epiblast*.—Stratified epithelium and cell perls (64) are present, besides trophoblast, and the carcinomatous areas which have been derived from Langhans' cells (62 and 65).

ii. *Mesoblast*.—The stroma is made up of fibrous tissue, in which there is a large amount of unstripped muscle and some cartilage (64). Case 65 also presents an appearance of endothelioma.

iii. *Hypoblast*.—Columnar and cubical epithelium lines some cystic spaces, into which it may project as papillæ. Structures resembling glandular alveoli are also present. Cases 63 and 65 show no derivatives of this layer.

There are, therefore, present the derivatives of the three primary blastodermic layers. It is therefore clear that these tumours are ordinary embryomata, and I need add nothing to what I have said in the last section as to their origin.

One layer in these tumours has always taken on an active growth, and has come to preponderate over the others. This layer is the epiblast. It is not the epiblast as a whole which has done this, but a special form of it, which resembles the trophoblast.

Until comparatively recently, chorion-epithelioma was only known to occur in the uterus as a result of pregnancy or abortion. It has been frequently observed after the expulsion of an hydatidiform mole. Maier, in 1876, was the first to note it. He described it as being a sarcoma of the decidua. Marchand, in 1895, recognised its epithelial nature. He, however, considered the syncytium to be of maternal origin. In 1903 he showed that both forms of cell are foetal and capable of assuming either form in response to different requirements. Teacher, in 1903, showed their relation to hydatidiform mole. Since then several cases of chorion-epithelioma have been described as occurring after pregnancy in other organs, the uterus being apparently exempt. Busse reports such a case in which the "primary" growth was in the heart.

It was not until later that these growths were described as occurring in the testicle. Kanthack, in 1897, adduces their occurrence in rapidly-growing sarcomata of the testicle as evidence in favour of deciduoma of the uterus being a sarcoma, and not metamorphosed uterine epithelium. It was not, however, until 1902 that Schlagenhauser showed that the testicular growths containing chorion-epithelium were really embryomata. He demonstrated the occurrence of derivatives of the three blastodermic layers of the embryo in them. About the same time Wlassow described several such tumours, but did not feel

justified in concluding they were chorion-epitheliomata, although he admitted that their appearance was identical. Since then many more such cases have been described, and the true chorion-epitheliomatous nature of these structures is now scarcely doubted.

I think I have established the fact that these tumours are embryomata, by showing the presence, in some of my cases at least, of derivatives of the three embryonic layers. I have already pointed out that one layer may grow at the expense of the others in these tumours. Usually this is the hypoblast. In chorion-epitheliomata, however, it is the epiblast.

There only remains, therefore, to discuss in which part of the embryoma the trophoblast originates, Schlagenhauser assumed that it is developed from the rudiments of foetal membranes, which he assumed to be present. Steinert attempted to show that the wall of an ovarian dermoid, which in many places is covered by pavement-epithelium, corresponds to the foetal amnion. Risel, however, demonstrated in a case of his that the chorion-epithelium arose directly from ordinary epiblastic epithelium. In his case this was neuro-epithelium. Several such cases have since then been reported. It would appear, therefore, that it is unnecessary to assume the presence of foetal membranes in this tumour, the trophoblast being able to develop from the ectoderm of the embryoma.

Comparison of normal and of pathological trophoblast.—It is a well-known fact that a chorion-epithelioma closely resembles the normal trophoblast. This is true, at least, for its early stages. The function of the normal trophoblast is to erode the maternal blood vessels, which lie in the deeper layers of the uterus, in order to derive the necessary nourishment for the growing ovum from them. In a chorion-epithelioma this eroding action is carried on to a much greater extent. The trophoblast bursts through many vessels and gives rise to extensive perivascular hæmorrhages. Its cells increase rapidly in number. They have not, however, got a sustaining connective tissue stroma with blood vessels. It is therefore clear that the cells must be able to nourish the new growths by abstracting nutritive material from

the blood. Else necrosis would be much more extensive than it is found to be. The syncytium is apparently able to do this, since it has been shown to contain hæmoglobin and loosely combined iron. The neighbouring tissues are in this manner deprived of food and undergo necrosis. In some sections which I have examined of a uterine chorion-epithelioma, the masses of trophoblast, which show no signs of degeneration, project into spaces filled with blood. Around these spaces are seen large areas of necrotic uterine tissue filled with leucocytes, whose function appears to be to remove the dead tissue. The trophoblast invades this tissue only to a very limited extent, its spread apparently taking place mainly by an extension along the blood vessels. The necrotic tissues seem to be removed mainly by the disintegration produced by the pressure of the masses of new growth and by the action of leucocytes. There is no evidence of the trophoblast enclosing and feeding on these tissues. The main difference, then, between normal and pathological trophoblast lies in its activity. Normally the invasion only takes place to a definitely limited extent along the blood vessels. Under abnormal conditions this invasion goes on to an unlimited degree. The cells of the new growth, which become detached, are also able to assume an independent growth in the blood vessels of distant tissues, giving rise to metastases. There is no difference in the form of the cells.

But cases 1 and 4 show large areas of a formation which resembles a carcinoma or endothelioma. The cells of this closely resemble the Langhans' cells. Small masses of syncytium can occasionally be seen between them. This appearance was described by Emanuel and Pick, who called it an *epithelioma chorio-ectodermale*. The trophoblast in this case seems to have lost the power of feeding on the blood of the host. It has got its own stroma with blood vessels. This is, indeed, scanty, but is always present. This appearance is in favour of the view that in embryomata the trophoblast is not developed from special fœtal membranes, but as a special form of the epiblast of the tumour, since the normal trophoblast, or that of a uterine chorion-epithelioma, has never been shown to be able to undergo any such change.

History.—The average age of the four patients at the time of operation is 26. The youngest is 20, the oldest 30. This is slightly younger than in the case of the other embryomata, in which the average is 29.

The average duration of the illness is well under a year, which indicates a rapid growth. Death occurred within a few weeks after operation in two cases. Case 64 had only been operated on six weeks ago, but he has already got an extensive metastasis. I have been unable to obtain an after-history of case 62.

Malignancy and metastases.—In the only case which I have been able to examine microscopically (65), metastasis took place through the blood, there being numerous deposits in the lungs and liver. One would expect that trophoblast would spread by the blood vessels. Unfortunately the abdominal glands, which were said to be enlarged, were not preserved. It is impossible to say if they contained trophoblast or other tissues of the embryoma.

In case 68 the spread again was by the blood vessels. Unfortunately the metastases were not examined microscopically.

SUMMARY OF CONCLUSIONS.

In the testicle, are found the following new growths:—

1. *Spheroidal-celled carcinoma.*—This is in nearly every case an encephaloid cancer. It may be alveolar or non-alveolar. It is often mistaken for a sarcoma. It may occur at a young age, and runs a clinically malignant course. Next to embryoma, it is the commonest form of new growth.

2. *Sarcoma*, which is usually, if not always, composed of round cells. It occurs at a somewhat earlier age than does carcinoma, and is even more malignant. It occurs far less frequently than is generally supposed. In young patients it may be bilateral.

3. There is evidence to show that carcinoma disseminates mainly by the lymphatics, and sarcoma by the blood vessels.

4. *Endothelioma*, which may arise in the endothelium of the blood vessels or lymphatics. It occurs usually in young adults, but may do so at any age. Although it generally runs a benign

course, it may be very malignant, and produce secondary deposits in the lymphatic glands.

5. *Embryoma*, which can be shown to contain structures derived from the three blastodermic layers of the embryo. It is the commonest new growth of the testicle, but it is often overlooked. Although not necessarily malignant, it may produce metastases composed of all the tissues of the primary growth. Or one tissue may become actively malignant, in which case the deposits will be formed of that tissue alone.

6. Some embryomata contain *trophoblast*, which can be shown to have originated in the epiblast of the primary tumour. In this case the trophoblast assumes malignant characters, the metastases being composed of the cells of this tissue alone. These tumours are very malignant, and usually occur in young adult life.

7. The trophoblast may assume a form resembling a carcinoma, sarcoma, or endothelioma.

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New Growths of the Testicle.

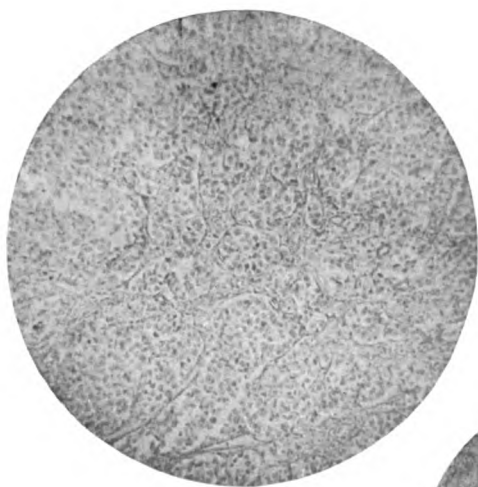


Fig. 1.

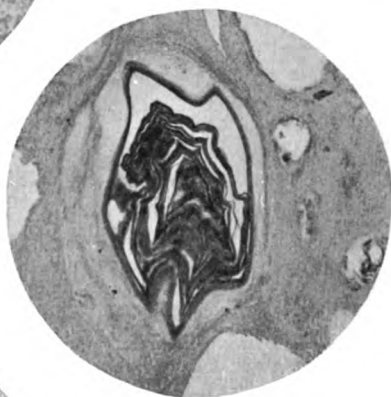


Fig. 2.

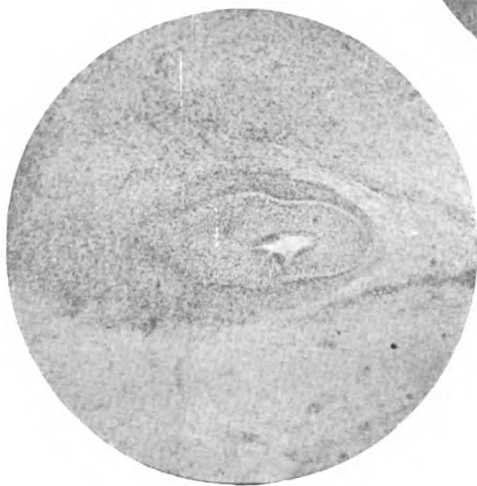


Fig. 3.

DESCRIPTION OF FIGURES.

Fig. 1.—Carcinoma. Alveolar variety. Case 13. Magnification 77. The whole figure is composed of groups of malignant cells arranged in alveoli, which are bounded by thin trabeculae of connective tissue (represented by black lines).

Fig. 2.—Embryoma. Case 47. Magnification 18. A developing tooth. The dark laminated substance of the tooth is well shown. It is separated in its upper part from the inner layer of the enamel organ, which can be traced all round the tooth as a dark line, which, under a higher power of the microscope, is seen to consist of cells. At the lower part of the organ there is an ingrowth of the stroma into it, forming a dental papilla.

Fig. 3.—Embryoma. Case 46. Magnification 40. Foetal spinal cord in testicular tumour. There is a somewhat irregular central canal, surrounded by a single layer of columnar ciliated epithelium (ependyma) with dark nuclei. Outside this there are many layers of neural epithelium, which is separated from the general stroma of the tumour by a layer of connective tissue, in which the cells are more abundant, and which therefore is dark in the figure.



THE PLACE AND VALUE OF SOME METHODS OF EXAMINATION OF THE URINARY ORGANS.

By R. P. ROWLANDS, M.S.

BEFORE undertaking an operation upon any of the urinary organs, the surgeon should of course ascertain the state of the general health of the patient, and he should also endeavour to gain all the information he can about the condition and functional capacity of each one of the urinary organs. It is especially important, before operating upon one kidney, to know the state and working capacity of the other. It is also desirable to know the value of the kidneys before operating upon any of the lower urinary organs. By means of more comprehensive examinations the surgeon may hope to make more accurate diagnosis, and to avoid useless and incomplete operations. Armed with a full knowledge of the separate and combined values of the two kidneys, the surgeon can more easily decide upon the extent of the operative treatment permissible in a given case, as well as the nature of the prognosis that may be given. On the other hand, valuable time must not be wasted on useless investigations, and vexatious and dangerous ones must not be undertaken unless they are likely to lead to important conclusions. In addition to the valuable information to be obtained from the history, symptoms, physical signs, chemical, microscopical, and bacteriological examinations of the urine, the catheter, and the sound, even more useful knowledge may be provided by other means in many cases.

Skiagraphy, cystoscopy, segregation, the estimation of the urea in the separated urines, and cryoscopy, may complete or confirm the diagnosis made by the older methods.

The surgeon must decide which, if any, of these comparatively new methods of investigation to use and rely upon in any given case. Some of them require special skill, and the value of others is as yet uncertain; but it is well to remember that we cannot afford to reject reliable information that can be obtained from any source, new or old, and that correct conclusions are generally made after careful consideration of all the available evidence without attaching undue weight to any one sign or symptom.

The object of this paper is to discuss very briefly the possible value and place of some of the most recent aids to the diagnosis of diseases of the urinary organs. Stress is laid upon some of the limitations and possible fallacies of the various methods, but no attempt is made to give a detailed account of the actual methods of examination, for space does not allow this.¹ A few cases are quoted for the purpose of illustration.

My grateful acknowledgments are due to my colleagues upon the Surgical and Medical Staff of Guy's Hospital for many opportunities of examining their patients.

The value of the X-rays in the diagnosis of urinary diseases.—The X-rays are capable of giving invaluable aid in the diagnosis of urinary diseases, but for reliable results a skilled radiographer, who has devoted much time and care to this method of investigation, is essential. He should also have a knowledge of anatomy, and clinical experience, to guide him in his work and guard him against mistakes. The evidence obtained by this means is not to be taken alone, but should be carefully weighed in conjunction with other facts, for by itself it may be misleading, like any other solitary sign. Mr. Shenton (*Lancet*, vol. ii., 1906, p. 719), in an able article upon this subject, rightly lays great stress upon the importance of screen examinations, and points out that photographs are of comparatively little value except as records of the objects which have been localised by means of the screen. A careful

¹ The techniques of cystoscopy and segregation are described by the writer in "The Operations of Surgery," Jacobson and Rowlands, Vol. ii.

and systematic examination of both kidneys, both ureters, and of the bladder, affords the only reliable and complete information. When a shadow has been discovered, a photograph may be taken as a valuable record of the position, number, and approximate size of the stones.

It can be safely stated that, with proper precautions, radiography is free of danger to the patient, and on this account, as well as that of accuracy, it compares very favourably with other methods of investigation, such as cystoscopy, segregation, and especially ureteral catheterisation. It is also more universally applicable, for cystitis, stricture, or enlargement of the prostate may interfere with or even prevent the use of these methods. Moreover, positive radiographic evidence of stone may make such examination superfluous. For these reasons, the evidence which the X-rays can afford should be obtained before resorting to the other methods which have just been mentioned.

That the evidence obtained from skilful radiography has become more and more accurate in the last few years must be the experience of every surgeon who is fortunate enough to secure the services of an experienced and capable radiographer, and the following remarks, from an excellent paper by Dr. Leonard (*Lancet*, 1905, vol. i., p. 1632), are well worth quoting upon this point:—" . . . The total amount of error in both the positive and negative diagnosis is less than three per cent. of the 330 cases examined. This is a percentage of error that compares very favourably with any other method, or all other methods, of diagnosis, including exploratory nephrotomy."

Mr. Shenton (*loc. supra cit.*) claims even greater accuracy, and the reader is referred to his paper for a valuable account of the methods of examination which have proved so successful in his hands.

It is fair to remark, however, that only a few experts can obtain such excellent results, and that even the best of them are human and liable to make mistakes, even with all the recent improvements in technique. I know of a patient whose kidney was explored with a negative result quite recently, and within a few days of an X-ray examination by an expert radiographer,

who had diagnosed a renal calculus, which was thought to be too large to have passed down the ureter between the examination and the operation. A few years ago the evidence, especially the negative evidence afforded by the Röntgen rays, was far from reliable, and unfortunately it often led the surgeon to advise against operation, or, more frequently, it encouraged the patient to refuse or defer an exploration until the kidney had become seriously damaged or even destroyed.

I may refer to two victims of such errors. One was a middle-aged man, whom I saw, with Dr. Faraker, about a year ago. Six years earlier the patient had attended a urinary hospital for symptoms which were suggestive of stone or tuberculosis of the left kidney. He was sent to a well-known radiographer, who failed to discover a stone, therefore an operation was not recommended. Believing that nothing more could be done for him, the patient did not seek further treatment until he had developed a large abscess in the left loin. During the six years that intervened the man had suffered much, and had become emaciated and sallow.

When I saw him he was too ill to allow a complete examination. When the abscess was opened it was found to extend from the bladder to the diaphragm, and to contain the kidney, which was full of stones, and so seriously damaged that it was at once removed. Primary nephrectomy was clearly indicated, for the exposed kidney was incapable of secreting any considerable amount of urine, and most of its vessels were afterwards found to be thrombosed.

A fortnight later, when the patient had recovered from his immediate danger, the left ureter was dissected out, from the postero-internal wall of the abscess, as far as the pelvic brim, just above which it contained a conical calculus one and a half inches long and a third of an inch in its greatest diameter. Above the stone the greatly dilated ureter contained a large amount of gritty phosphatic deposit. A few days later the patient got acute retention, due to an old-standing stricture, and then, as well as on several other occasions, urine freely escaped through the upper end of the left ureter. The patient made a slow but good

recovery, and before he left the hospital the amount of urine and urea excreted had greatly increased. Soon afterwards he resumed his usual work, which he has been able to perform ever since.

Another patient came from Ceylon only two and a half years ago to consult a distinguished urinary specialist in London. He was referred to a well-known radiographer, who failed to discover a stone, and in consequence of his verdict an operation was considered to be inadvisable, and the man returned to Ceylon, where he soon afterwards passed a small uric acid stone and much blood. Since then the pain in the right loin and along the course of the ureter got more and more severe, so that the patient recently returned to London and again consulted the same surgeon, who advised against another appeal to radiography, which he thought to be useless in this case on account of the reputed nature of the stone which had been passed. The diagnosis which was given was ureteral stricture, with retention of grit above it, and an operation was recommended. An instrument was to be passed through the urethra and bladder into the ureter, and to divide the stricture in the latter. The patient was to lie up for three days only. The urine was not examined. Later, the patient was sent to me, and was found to have pyuria and oxaluria. The right loin was very tender on percussion (Jordan Lloyd's test), but the ureter was not tender upon abdominal, pelvic and bimanual examination. Mr. Shenton found a large stone in the right kidney, and none elsewhere in the urinary apparatus, all of which was carefully screened. The total excretion of urea was satisfactory. The stone was removed from the pelvis of the kidney, the incision being made through the thinned cortex, because a more direct and easy access was thus gained, and the prospect of rapid healing without the formation of a temporary urinary fistula is greater with this incision. A catheter was passed along the ureter, which was neither dilated above nor constricted below, but normal in appearance and calibre. The patient made a good and rapid recovery. The stone was one inch long, three-quarters of an inch broad, and half an inch thick. Section showed it to be laminated,

and micro-chemical examination by Dr. Pembrey proved it to consist of uric acid, oxalates, phosphates, and blood pigment.

An incomplete X-ray examination is of no great value, and may be very misleading. Before undertaking a nephrolithotomy, for instance, it is not enough to know that there is a stone in one kidney without ascertaining the condition of the corresponding ureter and that of the opposite kidney and its duct. To gain this knowledge a complete examination of both sides is necessary, in addition to an estimation of the work done by each kidney (*vide infra*); failure to take these precautions may lead to an incomplete or even an unwise operation.

Even when a stone is discovered in the bladder it is quite likely that there is another at its probable source in one kidney or ureter, therefore a screen examination of these organs should be made.

The two following cases, which came under my notice when I was surgical registrar, illustrate this point:—

1. A man, complaining of symptoms of disease of the left kidney, had the left loin skiagraphed, with the result that a stone was discovered in and removed from the left kidney, which also contained pus. The patient died a few days later from uræmia and infection of the wound. Death disclosed the unsuspected fact that the right kidney was disorganised by multiple calculi.

2. An elderly man was greatly relieved by the removal of a stone from his bladder, but within a year another had to be removed. A few months later the man died from suppurative nephritis and uræmia. It was then discovered that both kidneys contained stones, although the patient had not complained of any renal symptoms.

Very small calculi may not be discoverable by means of the Röntgen rays, and therefore a negative result is not always conclusive, especially in stout patients. Uratic stones are also difficult to see, but calculi formed of urates or uric acid only are very rare, some phosphate or oxalate being practically always present in sufficient quantity to give a shadow. Mr. Henry Morris (*Lancet*, 1906, vol. ii., p. 141) has shown that xanthin and

cystin calculi are discoverable by means of the X-rays. Quite small oxalate of lime and phosphatic stones are opaque and easily recognised upon the screen.

Cretaceous mesenteric glands, phleboliths within the pelvic veins, atheromatous plates in the walls of the arteries, ossifying pelvic ligaments and tendons, and scybala in the colon, have all been mistaken for calculi. With greater knowledge and experience these mistakes are becoming quite rare; but the possibility of their occurrence should be remembered. In cases of doubt it is well to have two examinations, and it is always wise to give a purgative on the day before an examination is made so that faecal concretions may not mislead the radiographer.

Mr. Hurry Fenwick (*Brit. Med. Journ.*, June 17th, 1905), passes an opaque ureteric bougie in order to avoid such errors; this procedure is very difficult in the male, and not devoid of danger in either sex, but with these reservations it may be found useful in some cases.

The rays may give some information in other renal diseases; sometimes the kidney may be seen to be enlarged, for instance, or unduly fixed, suggesting a growth. It is especially important to remember that negative radiographic results should not be allowed to prevent or defer renal explorations which are strongly indicated by other evidence; this is especially true of unilateral hæmaturia of unknown cause; delay in a case of this kind may allow a renal growth to become irremovable before an exploration is undertaken.

Similarly, an operation for tuberculous kidney may be deferred until it is too late to hope for a good result, or a hydronephrosis, due to other causes than stone, may be allowed to damage the kidney irretrievably, if the surgeon does not bear in mind that other diseases of the kidney and ureter may give rise to symptoms which may closely simulate those of stone.

CYSTOSCOPY.

When it is used by an observer who is accustomed to it, and capable of interpreting what he sees, as well as conscious of

possible fallacies, the cystoscope gives invaluable aid in the diagnosis of diseases of the urinary organs from one another, and from other conditions.

For the safe employment of this valuable instrument, it is essential to conduct the examination gently and aseptically, so that neither hæmorrhage nor infection may be induced, and for the evidence which it affords to be reliable, it is necessary for the surgeon to have acquired skill in the use of the instrument, and a considerable experience of normal and abnormal cystoscopic views. The same bladder looks very different under various degrees of distension, for instance, and no two normal bladders are quite alike, and the same disease presents different appearances under various circumstances and at different stages.

For the introduction of the cystoscope the urethra must be large enough to admit a No. 22 French catheter, so that, when a stricture is present, it is necessary to dilate or divide this first, and when the meatus is unusually small, it must be enlarged. For obtaining a proper view the medium must be absolutely clear, and the bladder must be capable of holding at least four ounces of it. Growths, tuberculous and simple ulcerations, diverticulæ, calculi, vesical projections from an enlarged prostate, and a variety of other conditions may be seen through it, as well as valuable localising signs of renal disease. It must be used with judgment, and not indiscriminately, for any of these conditions. In many cases of enlargement of the prostate, for instance, the introduction of the instrument may be very difficult, or even impossible, so that more harm than good may follow its use under these circumstances, and especially if there is much cystitis. The diagnosis is frequently clear enough without the cystoscope, although, in certain cases, with little or no enlargement to be discovered from the rectum, the instrument is of real value, and it serves to exclude co-existing growth of the bladder.

The cystoscope is of great help in the early detection and careful examination of vesical growths, and thus it enables the surgeon to recommend an operation earlier than hitherto, and while the prognosis is still good. In other cases, it prevents useless explorations for inoperable growth. Dr. Stead, of

Hawkhurst, asked me to examine an elderly man who had vesical symptoms suggestive of stone or vesical growth. The sound had failed to discover a stone, but, as the patient had an enlarged prostate, the sounding was not considered to be conclusive. The cystoscope disclosed an infiltrating and extensive flat growth of the base and left side of the bladder. A radical operation was out of the question, and there was no indication for palliative drainage, for there was no obstruction of the urethra. The old man was saved a journey to London and a useless exploratory operation, which would probably have left him with a urinary fistula. He died about three months later. In a similar way, a hopeless operation was avoided in an old lady who was sent by Dr. Wynne, of Northiam.

In hospital practice it is unfortunately rare for the subjects of malignant disease of the bladder to seek treatment early enough for a radical operation to be undertaken hopefully.

The early use of the cystoscope is strongly indicated in cases of symptomless hæmaturia, for the source of the bleeding, which must otherwise be uncertain, can be ascertained with great accuracy with this instrument. Not only can we decide between renal and vesical causes of hæmaturia, but if the examination is made during the progress of the bleeding, the blood may be seen to issue from one or other ureter.

A good example of the value of the cystoscope is a case of villous tumour, which was situated at the left ureteral orifice, and had given rise to hæmaturia associated with pain in the left loin, suggestive of renal calculus. A fruitless lumbar exploration was avoided by the examination.

The cystoscope may enable us to define the nature, size, number, position, and character of the basal attachment of vesical growths, and also the presence or absence of infiltration of the vesical wall. Hence the knowledge gained by a careful use of this instrument may indicate the exact nature and degree of the surgical interference that may be required, so that the surgeon can adopt the most suitable method without waste of time during the actual operation.

In some cases with infiltration of the bladder base, which is palpable from the rectum, it is not necessary to examine the interior of the bladder, for the time for radical operative interference has already passed.

In certain cases hæmorrhage may be so profuse, in spite of all gentleness, injections of adrenalin, nitrate silver, &c., that the cystoscope may fail to give any information of value. It is wise to wait for an interval in these cases, the patient being kept at rest in bed, and when the urine is clear again the bladder may be examined through this medium to avoid the risk of setting up fresh hæmorrhage by irrigation, but if the bladder contain any appreciable amount of pus or mucus it is not possible to examine it satisfactorily without irrigation. In some cases an irrigating cystoscope may be of great help when oozing persists in spite of all endeavours to check it, but quick work with an ordinary Nitze's examining cystoscope will succeed unless the bleeding is profuse. Hæmorrhage is likely to be troublesome with friable growths, which surround or grow near the vesical orifice of the urethra; bleeding from over-distension and rough handling is avoidable. On account of the well-known tendency of all vesical growths to recur, it is wise to examine these patients cystoscopically at regular intervals for some time after the removal of the growths: in this way only can recurrences be discovered early and treated hopefully.

The cystoscope is useful in making or clinching the diagnosis of tuberculous cystitis, and in showing the extent and position of the disease. In rare cases the ulceration may be seen to be localised enough to justify operative interference, but usually the cystoscope reveals widespread disease, for which experience has shown that operations are worse than useless as a rule. Tuberculin is now being hopefully tried for these cases, but how far events will justify the optimistic views prematurely expressed by some is uncertain.

In other cases the disease may chiefly affect the neighbourhood of one ureteral orifice, then probably indicating primary disease of the corresponding kidney, with secondary infection of the bladder, but this is not always so. I have known a patient whose

right kidney had been thoroughly explored and incised with a negative result for pain in the right loin, pyuria, and frequency of micturition. Later, tuberculous disease of the bladder, involving the right ureteral orifice, was seen through the cystoscope, which, if it had been used earlier, might have prevented a fruitless operation. The frequent use of the cystoscope for tuberculous disease of the bladder is to be condemned, for instrumentation of every kind is detrimental, and to be avoided as far as possible.

Occasionally the sound fails to discover a stone in the bladder, although the symptoms may strongly suggest the presence of one. In such cases the cystoscope may reveal tuberculous disease, epithelioma, or a stone, which is encysted or too soft or small to give the characteristic ring with the sound. Calculi impacted at the vesical end of the ureter and giving rise to vesical symptoms have been discovered and localised by means of the cystoscope. I once mistook a nodular stone which was partially encysted in a bleeding bladder for a sessile papillomatous growth. Such a mistake, although excusable under the circumstances, is certainly avoidable, but I mention it as a warning to others.

The cystoscope may be very useful in deciding between renal and vesical disease, and between right and left renal disease; thus the source of hæmaturia or pyuria of doubtful origin may be clearly defined, for a skilful observer may see blood or pus issuing from one ureter, or he may notice an ulcerated, retracted, or dilated ureteral orifice, indicating the side of the renal disease.

Before operating upon one kidney the cystoscope affords the most certain available means of proving the presence of another one. The hand in the abdomen is well known to be unreliable, for the most capable surgeons have been misled by this method, the spleen having been mistaken for a kidney, for instance. Moreover, if a kidney is really and certainly felt through the peritoneum, neither its presence nor its size can possibly tell us that it is either healthy or even doing any work, for the ureter may be blocked and the kidney hydronephrotic, or the subject of tuberculosis or growth. Proof of the rhythmical discharge of normal urine out of the corresponding ureter is far more reliable.

In differentiating between renal and other abdominal enlargements, the cystoscope is sometimes useful, even apart from the appearance of any abnormal constituent in the urine. For instance, a pancreatic cyst may simulate hydronephrosis or pyonephrosis, but if healthy urine issues freely from the ureter of the suspected kidney, hydronephrosis is very unlikely, and pyonephrosis can be absolutely excluded.

SEGREGATION.

A reliable segregator or separator (Luy's) may render valuable aid by enabling us to collect and examine the urines from the two ureters separately.

(a) Blood, pus, or even the cells of growth, may come from one side only, indicating the side of the disease. Microscopic quantities of these products can be discovered in one of the separated urines after the cystoscopic examination has failed to show any difference.

(b) The amount of urea coming from each kidney may be estimated, and thus the diseased organ may be determined, and roughly the comparative value of the two kidneys, supposing both to be diseased, as proved by the discharge of morbid urine from both ureters. The freezing points of separated urines may also be obtained.

(c) Similarly the amount of sugar coming from each kidney in the Phloridzin test may be determined, and also the amount, time of onset, and duration of the elimination of chromogen in the methylene blue test; urine of different degrees of colour may flow from the two tubes.

(d) It may enable us to distinguish between renal and other enlargements or diseases; thus, if normal urine issues from the suspected kidney, a swelling in the neighbourhood of the kidney is proved to be other than renal, but if little urine, or only pathological urine, escapes from the corresponding ureter, the swelling in the loin is probably renal. Again, pain in the loin and shooting along the ureter is not likely to be due to renal disease if the urine collected from the corresponding ureter is

normal in amount, and contains its proper share of urea, but no pathological products.

(e) It may help us to find out whether unilateral, primary, or idiopathic nephritis really ever occurs, as some would have us believe.

It must be remembered, however, that a considerable amount of skill and anatomical knowledge are required for the proper and safe use of the instrument, which may be very misleading, or even dangerous, if carelessly handled; thus, a case has been recorded in which urine came from both sides of the segregator, although the patient only possessed one kidney. It is easy to understand that a slight relaxation of pressure on the bladder base may allow urine to pass the india-rubber diaphragm from one side to the other. The instrument is not at all easy to introduce in the male, because its size is larger and its shape more awkward than that of the examining cystoscope. The curve of the instrument may get arrested below the pubic arch, with the point only just within the bladder, or the urethra may be severely lacerated unless skill and gentleness entirely replace rough or clumsy usage. No bleeding must be induced either in the urethra or bladder, for blood may block one or both tubes, and interfere with the accurate working of the instrument. Unless the separator is kept perfectly still after it has been applied, and the contents of the bladder have run away through the tubes, the mucous membrane may be abraded and hæmorrhage induced, probably to one or other side of the membranous partition. Clots may then partially or completely obstruct one of the tubes, and this may lead to serious error, for blood-stained fluid may flow into one receiver and be considered to issue from the corresponding ureter, or little or no urine may escape from one tube. The surgeon may remain in ignorance of this source of error until the end of the examination, when he tests the patency of the tubes again.

It should be remembered that the segregator is neither safe nor reliable unless the bladder has been first examined with the cystoscope, and seen to be free of disease, for a villous growth, carcinoma, encysted stone, or inflamed pouch, might add morbid

products to the urine of one side only, and this might lead to serious mistakes. Moreover, the instrument might inflict grave injury if carelessly introduced into some diseased bladders. Apart from obvious difficulty in its introduction, it cannot be relied upon in patients with vesical projections arising from enlargement of the prostate, for the base of the bladder may be too uneven. It should not be used in cases of contraction of the bladder due to carcinoma or late tuberculosis, and it cannot be passed in cases of urethral stricture until the latter has been dilated or divided. It is sometimes necessary to incise a narrow meatus.

If the urine contains pus it is always necessary to irrigate the bladder well, both to allow the preliminary cystoscopic examination, and to guard against the possibility of obstruction of the tubes from stringy pus retained at the base of the bladder; it is also necessary to take this obvious precaution to guard against sepsis.

It is essential for the patient to be in a semi-sitting attitude during the separation, and for this reason, as well as that of freer secretion, it is wise to conduct the examination under cocaine anæsthesia, although the introduction of the instrument is certainly easier with a general anæsthetic.

Although the segregator needs careful handling and has certain limitations which I have briefly referred to, it has the advantage of being much easier to use than cystoscopic ureteral catheterisation in the large majority of cases, and for the majority of clinical surgeons who require to collect the secretions of the two kidneys separately.

Ureteral catheterisation is a very difficult and tedious procedure, which is not free of danger even in practised hands, and it is now rarely necessary for the separation of the urines for diagnostic purposes, for the segregator provides a simpler and safer means of attaining this desirable object. Further, the ureteral catheter may give misleading results, for the instrument may get blocked, or its orifice be obstructed with mucous membrane, and it is common for the ureter to bleed a little from slight injury to its mucous membrane, inflicted during the introduction of the instrument, and obviously this may lead to grave

error. The danger of infecting a healthy kidney from a diseased bladder has been exaggerated, but it does exist, and cannot always be evaded by care. Even Kelly's far safer and comparatively simple direct method of catheterising the female ureter is not so easy as segregation, and the former disturbs the patient and the bladder more.

The determination of the functional capacity of the kidney.—Dr. Ashton Berg (Annals of Surgery, May, 1906, p. 726) has contributed an able discussion upon this important subject, and much of what follows has been derived from his paper. He points out that the problem is a threefold one; we want to discover the amount of—

(a) The combined work of the kidneys; (b) the individual work of each, and (c) the probable amount of work that each is capable of doing if its fellow is excised or seriously damaged.

(a) The combined work is estimated from (i.) the cryoscopic index of the blood, and (ii.) the amount of urea discharged in twenty-four hours.

(b) The individual work is determined from (i.) the percentage of urea in the individual urines, and (ii.) the amount of sugar and chromogen in each urine after an injection of phloridrin and methylene blue, (iii.) and the cryoscopic index of each urine.

(c) The potential functional power of each kidney cannot be estimated with any degree of accuracy from the results of a and b.

CRYOSCOPY.

Koranyi was the originator of this method of investigation, which aims towards estimating the functional capacity of the kidneys by means of determinations of the freezing points of the blood and urine.

Kümmel, Rosving, and others, have written much upon the subject. (German Surgical Congress, 1905, *Lancet*, vol. i., p. 536.)

The cryoscopic index of the blood.—The freezing point of normal blood is from 0.56° to 0.60° C. below that of distilled water. When the solids increase from deficient renal excretion, the freezing point falls below 0.60° C., and it also falls in certain diseases accompanied by deficient oxidation, such as large

abdominal tumours, cardiac and respiratory insufficiency, etc. In severe anæmia the blood is so thin that considerable retention of potential urinary excretions may occur without a fall of the freezing point below 0.60°C .

Dr. Berg concludes that "the cryoscopic index of the blood merely indicates the work that is being done by the renal organs. *It teaches us nothing of the health or disease of the kidneys*, for three-fourths of the total kidney-tissue may be destroyed, and yet the remaining one-fourth will be sufficient to maintain the normal molecular concentration of the blood; nor does it afford an indication of their potential functioning power. Only in connection with the health or disease of the individual organs can the freezing point of the blood be considered as a help in this respect."

"(a) A normal cryoscopic index of the blood, when there is one healthy and one diseased kidney, would indicate a potentially sufficient functional capacity of the sound organ, and would warrant us in doing a nephrectomy.

(b) An abnormally low cryoscopic index of the blood, when there is one healthy and one diseased kidney, does not indicate potential insufficiency of the former, for the function of this organ may be only temporarily impaired by the diseased fellow-organ. In such a case nephrectomy may nevertheless be done safely.

(c) A normal cryoscopic index of the blood, when there is one slightly diseased and one extensively diseased organ, would usually point to a potentially sufficient functional capacity of the less diseased organ, and would allow of our doing a nephrectomy or other operation upon the more affected kidney.

(d) A normal cryoscopic index of the blood, when there is more or less extensive affection of both kidneys, does not mean a potentially sufficient functional capacity of these organs, and does not permit of our removing one, or even incisively attacking either organ.

(e) An abnormally low cryoscopic index of the blood, with more or less extensive disease of both kidneys, indicates their potential insufficiency, and strongly speaks against the advisability of doing any operation upon them."

From the above it is clear that too much reliance must not be placed in this one source of information, and to reject all patients with a freezing point of the blood below 0.60° C. as unsuitable for nephrectomy, or major operation, is absurd. Dr. Berg has performed nephrectomy when the freezing point has been as low as 0.65° C. and 0.67° C., and the patients have recovered.

The cryoscopic index of the combined urines is of far less value, because the freezing point of the urine normally varies from 1.2° to 2.2° C. below that of distilled water. This is due to variations in the circulation, nervous influence, and especially the amount of fluid partaken. If the freezing point falls below 1° C. under normal conditions, renal excretion may be assumed to be deficient.

A comparison of the freezing points of the separated urines may, however, be valuable, and may indicate the proportion of the work done, and with less certainty the comparative amount of renal tissue in the two kidneys.

Estimation of the average total amount of urea passed in the twenty-four hours is of value; it should be about 350 to 400 grains in a healthy person in bed on farinaceous diet. If it is below 300 grains renal insufficiency may be assumed. Mr. Clement Lucas, many years ago, relying upon this test, refrained from removing a seriously damaged tuberculous kidney. The patient died of diphtheria, and was found to have only one kidney.

A comparison of the percentage of urea in the separated urines is of more value, for it enables us to tell which is the diseased, or the most diseased, of the two kidneys.

Rosving relies upon this and a careful examination of the separated urines, and he "maintains that a kidney which secretes healthy urine containing a normal percentage of urea is functionally sufficient, and may be relied upon to satisfactorily perform the full work of the body."

The Methylene blue test.—The bladder being empty and the segregator or ureteral catheters introduced, a sterilised solution of 0.05 grm. of methylene blue may be injected beneath the skin of the flank. The urines from the two ureters may soon differ in

colour. The time of onset, the rapidity and duration of the elimination by each kidney, should be estimated, and from these data the comparative functional capacity of the two kidneys may be inferred.

The Phloridzin test.—Phloridzin (0.005 grm.) is injected subcutaneously, and the amounts of sugar appearing in the separated urines is estimated, and from a comparison of these amounts the functional activity of each kidney may be inferred.

These tests are of little value in determining the potential functional capacity of the kidneys, except when the state of the kidneys as regards presence or absence of disease is known from other sources, such as a thorough examination of the separated urines.

In conclusion, it may be stated that valuable information may be obtained by a careful, skilful and combined study of—

- (1) The cryoscopic index of the blood.
- (2) The percentage of urea in the separated urines.
- (3) The chemical, microscopical and bacteriological examination of the separated urines.
- (4) A comparison of the freezing points of the separated urines.
- (5) The average total amount of urea passed in the twenty-four hours.
- (6) Rate of excretion of methylene blue and sugar in the methylene blue and phloridzin tests.

The urines should be separated as a rule by means of the segregator, and not by ureteral catheterisation, which Berg, Rosving and others recommend.

The following case may serve to show the value of some of the modern methods of diagnosis of urinary disease. A middle-aged man was admitted into Guy's Hospital, under the care of Sir Cooper Perry, suffering from attacks of hæmaturia. The bleeding was profuse and painless, but it lasted only for a few hours at a time. In the intervals the urine was healthy. There were no abnormal physical signs in the loins or along the course of the ureters; there was some dull pain over the sacrum. A radiographic examination was negative, except that the renal shadow

was larger than normal. On examining with the cystoscope I proved the absence of villous or other growth of the bladder, and found the bladder to be normal except for a slight enlargement of the right ureteral orifice and some congestion around it. The patient never had an attack of bleeding when in the hospital, although he was encouraged to take exercise and to go up and down stairs: and bimanual pressure in the loins failed to send any blood down the ureters during cystoscopic examination. Later the man returned, bringing with him a ureteral cast, and he had a slight varicocele on the right side.

The segregator was introduced, and the urine issuing from the right side was paler than that from the left, and the latter contained 2·3 per cent. of urea, while the former only had 1·3 per cent. Control examinations gave similar results. The centrifugalised right urine showed crenated red blood corpuscles and large round cells of growth, whereas the left urine was normal. Cryoscopic examination of the separated urines by Dr. Bell Walker confirmed the conclusion that the right kidney was doing much less work than the left. The total amount of urea was satisfactory. A diagnosis of growth of the right kidney was made with confidence, and this was proved upon exposing the kidney, which was fairly fixed by peripheral inflammation and hidden high up in front of the ribs. The kidney was removed without hesitation, for the other one was known to be doing its work very well. The patient unfortunately died from lobar pneumonia of the left lung a few days later. The wound was doing well, and there were no secondary growths anywhere. The neoplasm was encapsuled, and occupied the middle two-thirds of the kidney, bulging irregularly upon the cortex and projecting into the pelvis and the beginning of the ureter, where its surface resembled the colour of the yellow oxide of mercury.

Microscopical examination by Dr. Nicholson proved the growth to have originated from an adrenal rest. It is rare for this type of growth to invade the pelvis and cause hæmaturia.

A young married lady, a patient of Dr. Webster, of Heathfield, was sent to me towards the end of the year 1906, for symptoms which had suggested disease of the right kidney. Seven years

earlier the vermiform appendix had been removed and had been found to be diseased and unusually long and distended. The operation brought relief, but when the patient began to go about again she suffered from pain in the right loin and groin, so that she was not able to take any active exercise.

She noticed the pain on standing, sitting, or on turning over to the left, and any jolting made it much worse; relief was usually obtained by lying down.

Sometimes the patient got blanched, and felt faint during the pain. Undue frequency of micturition was noticed both during and after each attack of pain. An obstetric physician was consulted two years ago, and he thought that the right ovary was enlarged, but not enough to need any interference at that time. The attacks became more frequent and more severe, and there had been unusual pain during the early part of menstruation of late. In May and June, 1906, the patient had to rest on account of mucous colitis. In July, 1906, Dr. Webster found pus in the urine, and soon afterwards a surgeon saw her, and, believing that most of the symptoms were due to hysteria, he advised against operation. The right kidney and ureter had been skiagraphed several times with negative results.

When I examined the patient the right kidney was not movable, and there was no tenderness in the loin. The appendicular region was unduly tender on deep palpation. The urine was normal, there was no pus, and no abnormal constituent in a centrifugalised specimen. The patient was admitted into the private ward for observation, the urine being examined daily and the amount of urea estimated and found to be nearly normal. The patient was asked to walk up and down the ninety steps leading to Bright Ward, but this gave rise to so much pain that she was glad to desist. Cystoscopic examination showed that urine issued from each ureter, and that the bladder was not diseased in any way. The specimens obtained by segregation were normal, and the urine from the right tube contained a little more urea than the left.

It was therefore quite clear that the symptoms were not due to vesical disease, and that both kidneys were doing good work

so that it was very unlikely that there was anything wrong with either of them. Without the knowledge derived from the cystoscope and the segregator, it was uncertain if the right kidney was acting at all, for the left one might have hypertrophied and be the source of all the urine passed. A complete or nearly partial obstruction of the right ureter might have accounted for the symptoms.

Upon bimanual examination, the right side of the pelvis was slightly fuller and far more tender than the left. The abdomen was opened through the lower part of the right rectus muscle. A broad band of fibrous tissue was seen starting from the right flank near the parietal scar, and extending obliquely across the ascending colon to the mesial aspect of the latter, where it was attached to the parietal peritoneum. The band was divided, and the hand was passed up to the right kidney, which was of normal size and not movable. No stones could be felt in the gall bladder, which was not distended. The cæcum was found to be unusually large, and to lie entirely in the true pelvis. The appendicular site was quite smooth and even, but easily discovered by following down the anterior longitudinal muscular band. The right ovary was adherent, and about three times as large as the left one, which was normal. The right ovary was therefore removed, consent having been previously obtained, if this step proved to be necessary. The capsule was dense, white, and very thick, evidently as the result of old peritonitis, which had probably spread from the diseased appendix close by. The gland consisted of two cysts and a dense fibroid stroma. The abdominal wound was closed, the rectus sheath being overlapped to prevent the occurrence of ventral hernia. The patient made a rapid recovery, and is now able to go about and take active exercise without any pain or inconvenience.

The indications of right renal disease were very misleading in this case, as is shown by the repeated X-ray examinations which were recommended. The source of the pus remains uncertain, but it was probably vaginal.

CERTAIN FEATURES CHARACTERISTIC OF TELEOSTEAN DEVELOPMENT.

By RICHARD ASSHETON, M.A.

(Re-arranged from a Short Course of Lectures given at
Guy's Hospital, March, 1907.)

ALTHOUGH I have left these lectures in lecture form, I have been obliged to modify the arrangement. Many diagrams have been omitted, and some of the more elementary matter has been condensed; while in one or two cases I have expanded the sections which are more controversial in character.

Special reference is made to the development of the Mormyroid Teleostean *Gymnarchus niloticus*, the eggs of which were discovered and collected in the Gambia river in 1900 by the late Mr. John Samuel Budgett, M.A., F.Z.S. It has been my privilege to work out the development of this fish from his material, and a fuller account of the results will be found in the memorial volume of Budgett's work published by the Cambridge University Press.

Figures 11, 12, 14, 15, 17 are from my paper on the development of *Gymnarchus* published in the Budgett Memorial volume, and I desire to thank the Syndics for their kindness in lending me the blocks of these figures.

INTRODUCTION.

In development, as in the adult forms of animals, we may find features which are peculiar to the species, group, or class

which we are studying. Such, for instance, are the enlargement of the urinary bladder to form an organ of respiration in the Amniota; the rejection at birth or before birth of some part of the yolk sac in the Mammalia; the separation of the epiblast from the yolk after the laying of the egg in the Aves; ciliated ridges or tracts on the larvæ of many invertebrates, and so on. These are features of great developmental importance, and are so constant that they may be said to be *diagnostic* of the group or class under examination.

But these features are comparatively rare. More often there are features which are found generally in a group, and yet may not be confined to that group, or which, though usually occurring, are not universally present within the group, and so cannot be described as *diagnostic*, although they may be said to be characteristic of the group.

So, when considering the development of Teleostean fishes, the question naturally arises whether there are any features of development which can be said to be diagnostic or even characteristic of Teleosteans.

I think it will be well to try and answer this question at once, and to point out what features may be thus described.

As diagnostic characters, I may suggest—

1. The cutting off of part of the cœlom in which the nephrostomes and glomus of the pronephros lie, to form the “pronephric chamber.”
2. The complete absence in both sexes of any connection during development between the kidney tubules and the reproductive system. (It is true that at a late stage in some cases the reproductive ducts open into the urinary duct close to the cloaca; but such communications are of a different nature to those referred to here.)
3. The growth backwards of the air-bladder (or lung) above the abdominal cavity—that is to say, between the peritoneum and kidney, with which, probably, the character just mentioned is correlated.

In addition to this, there are others which are at any rate characteristic from various points of view.

1. The small size of the egg in combination with a meroblastic segmentation.
2. The separation of the embryonic rudiment from a covering layer at an early stage, sometimes, though probably erroneously, spoken of as a division into ectodermic and nervous layers of the epiblast.
3. The combination of meroblastic segmentation with very rapid and even overgrowth of the yolk by the lips of the blastopore.
4. The intensity of the stretching which the "embryo" undergoes by the yolk mass during the earliest stages which, with the accompanying delay in formation of a head fold, causes, for a much longer time than in other vertebrates, the displacement of the heart rudiment anterior to the head of the "embryo."
5. The entirely venous nature of the supply of blood to the yolk sac throughout embryonic and larval life.
6. "Kupffer's vesicle."
7. The formation of a syncytial layer of protoplasm with large nuclei next the yolk, the so-called periblast; this at first is continuous with the covering layer mentioned in paragraph 2.
8. Participation of the ectoderm in the formation of the gill-clefts.
9. Epiblastic nature of gill filaments.
10. Absence of or early closure of the hyomandibular cleft.
11. Small degree of cranial flexure.
12. Formation of the neural tube and optic and auditory vesicles from solid rudiments.
13. Failure of the corpora striata to form concavities on their inner surfaces; hence no lateral ventricles occur in the brain in the adult.
14. Slight development, or absence, of the paraphysis.

SEGMENTATION OF THE OVUM.

The egg of Teleosteans varies much in size; it may be, as in most of the pelagic ova, quite small, measuring not more than

·3 mm. (Eigenmann (7)), or it may be, comparatively speaking, large in the demersal type, like those of the salmon, or of *Gymnarchus* (Budgett (4)), one of the Mormyridæ, in which it measures 10 mm. in diameter, or it may be, as in *Arius commersonii*, as large as 18 mm. in diameter.

But no matter what the size of the ovum may be, the type of segmentation and mode of formation of the embryo is extraordinarily uniform throughout. The most striking character of the segmentation is the very sharp separation that occurs between the yolk and the protoplasm, which results in the formation of a well-defined cap of cells lying on the yolk mass which has only a thin superficial layer of protoplasm upon which the cap of cells lies.

The egg is nearly always bounded by a tough egg membrane, sometimes called zona radiata, which is often perforated by many fine pores and has a larger aperture, the micropyle, through which the spermatozoon enters. This shell or membrane is said by some to be formed by the yolk, in which case it should be regarded as a vitelline membrane. It seems, however, possible that it may be formed by processes of the follicle cells (granulosa layer) which perforate the zona forming the small pores just mentioned. Other thinner membranes may occur outside it.

Before fertilisation the protoplasm is more evenly distributed in the yolk (Henneguy (12)), but on fertilisation the protoplasm becomes concentrated at one pole, so that this pole, the germ disc, alone segments, the rest remaining throughout its existence as an inert mass of food yolk.

The segmentation begins in all cases by two vertical furrows, at right angles to one another, which may or may not penetrate to the bottom of the germ disc. From this point there is considerable irregularity. The result, however, is always a cap of blastomeres lying on a syncytial layer, to which the name periblast has been given (v. Kopsch (20), Hertwig (14), Gudger (11), etc.)

This periblast layer contains nuclei round the periphery and in the middle, though usually they are absent from the centre at first, which difference depends partly upon how far down the first segmentation furrows pass through the germ disc.

The periblast differentiates either by the fusion of the lowest of the segmentation cells to form a plasmodium, or more often it forms by the failure of the lowest layer of the disc to segment, in which case there is a plasmodium from the start. In each case the nuclei, after some multiplication, cease to divide and become hypertrophied, giving rise to the large yolk nuclei characteristic of later stages. So long as any small nuclei remain, they may divide and give rise to additional embryonic cells.

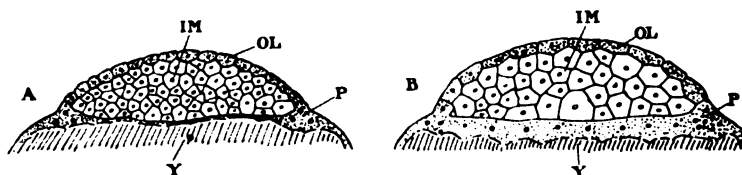


Fig. 1.—Diagrams to show the upper part of a Teleostean egg at the close of segmentation.

- (A.) When the yolk nuclei are at first absent from the periblast in the centre.
- (B.) When the yolk nuclei are present in the centre as soon as the layer is differentiated.
- (IM.) Inner mass from which the whole embryo is formed.
- (OL, P.) Covering layer and periblast which form a "trophoblastic" envelope.

The periblast, thus differentiated from the rest of the blastomeres, henceforth takes no part in the direct formation of the tissues of the embryo (Fig. 1). Moreover, the periblast layer is directly continuous with the superficial layer of the cells of the segmented disc. This superficial layer retains the connection for a long time and never behaves as an epiblast. It is a special covering layer, and is characteristic of the Teleostean embryo, and must not be confounded with the ectodermic layer of epiblast of the Anura, which is an early separation of spongioblastic from neuroblastic elements.

The Teleostean covering layer, together with the periblast, form a protective and nutritive investment quite analogous to the trophoblast of eutherian mammals.

COMPARISON OF THE SEGMENTED EGG OF A TELEOSTEAN WITH
THOSE OF SOME OTHER VERTEBRATES.

We may compare the eggs of an Amphibian, Teleost and Amniote at this stage :—

<i>Amphibian.</i>	<i>Teleostean.</i>	<i>Amniote.</i>
Holoblastic.	Meroblastic.	Meroblastic.
Segmentation cavity large and of long duration.	Segmentation cavity insignificant and transitory.	Segmentation cavity insignificant and transitory.
Gradual mergence of cells of upper layers with yolk cells.	Sharp separation of cells of upper layers from yolk cells.	Mergence of cells of upper layer with yolk cells, though more sudden than in Amphibian.
	The yolk cells, together with the outermost layer of segments, form an investment which probably takes no direct part in the formation of the tissues, but is of the nature of a protective and nutritive envelope.	In Eutherian Mammals the outermost layer of segments form an investment which takes no direct part in the formation of the adult, but is of the nature of a protective and nutritive envelope.
Gut cavity formed early and open to exterior by blastopore from the beginning.	Gut cavity formed early, but temporarily obliterated except for Kupffer's vesicle, and seldom open by either blastopore or neurenteric canal.	No true blastopore, but neurenteric canal of later times may afford an opening to the gut cavity, which is formed early as a subgerminal cavity.

COMPARISON OF THE TELEOST EGG WITH THE ELASMOBRANCH.

The eggs of Elasmobranchs and Teleosteans are alike in being meroblastic, but the eggs of Elasmobranchs are much larger than most Teleostean eggs, so that the segmenting portion, instead of forming a raised cap, lies sunk down into the large yolk mass, a condition which is seen, however, in the large egg of the Teleost *Gymnarchus*.

There is a sharp distinction into embryonic segments and yolk which contain large nuclei similar to those of the Teleost periblast, but which, according to Rückert, have a very different origin.

Two obvious cavities occur during the early stages of development of the Elasmobranch egg. The first is small and, according to some writers, it disappears early. This is called segmentation cavity by R. Hertwig (14). According to others, it shifts its place, but gives rise directly to the second and much larger cavity, which is apparent at the close of segmentation, and which was called segmentation cavity by Balfour. To this Rückert applies the term Keimhöhle.

In time and mode of origin this later cavity resembles the subgerminal cavity of Amniota and the large cavity appearing at the end of segmentation in Teleosteans which seems to correspond with the subgerminal cavity; but there is no evidence that it ever forms part of or becomes continuous with the gut cavity. Hence one is inclined to regard it as segmentation cavity, and to favour the view that it and the earlier apparently transitory cavity are conterminous.

FORMATION OF THE TELEOSTEAN "EMBRYO."

After the segmentation of the ovum there is a gradual spreading of the cap of cells in all directions. This is accompanied by a general thinning out of the cap and the appearance of a cavity between the segmentation spheres and periblast, or segmentation spheres and yolk, in those cases in which the periblast is not formed till later. The whole structure is still roughly radially symmetrical; at any rate, there is no marked bilateral symmetry.

This moment corresponds to that time in amphibian development just before the dorsal lip begins to grow over the lower part of the egg, and in the bird or mammal to the time immediately before the appearance of the primitive streak, *i.e.*, before the growth in length has started.

This cavity in the Teleost, then, probably corresponds to the true archenteron and is homologous to that part of the gut cavity of the Amphibian, which forms by splitting or by invagination, and that in the bird or reptile, which is called the subgerminal cavity.

As seen in surface view, the cap of cells expands, and at one point of the periphery a knob-like thickening occurs (Fig. A).

This "knob" is the mid-dorsal region of a circular band of specially active tissue, which whole band is a secondary growth centre, arising eccentrically to the primary growth centre, and which by its activity gives rise to the increase in length of the embryo, and induces a marked bilateral symmetry. The knob itself is only the mid-dorsal area of the whole circular band of proliferating tissue. One speaks for convenience of "the embryo" and "blastoderm" as though they were independent structures, but it should be borne in mind that the blastoderm is really the ventral wall of the embryo much distended by the yolk mass. This is of importance, as will appear in the subsequent discussion of the theory of concrescence.

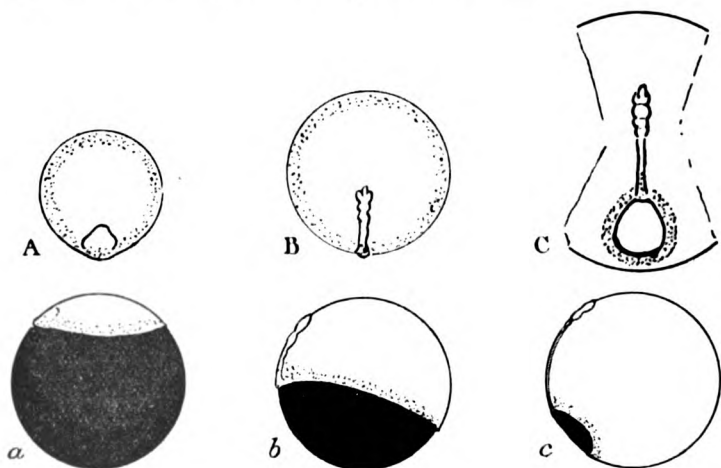


Fig. 2.—Diagrams illustrating the spreading of the blastoderm over the yolk in a Teleostean egg.

(A, B, C,) Surface views of the "embryo."

(a, b, c,) The same in side view, showing also the yolk mass.

The cellular disc expands rapidly, so as to travel over and cover the whole yolk mass, and the edge of the disc, which must be regarded as the lip of the blastopore, increases in circumference until the equator of the yolk has been attained (Figs. Aa, Bb), and

afterwards diminishes (Figs. Cc) until a coalescence results in the complete disappearance of the yolk mass from the surface and, therefore, closure of the blastopore.

In the mid-dorsal line and dorso-lateral margins this edge is a typical blastopore lip, where epiblast and hypoblast are continuous; but certainly in some species (*e.g.*, *Batrachus Tau* (Clapp(6))), the ventral and ventrolateral parts of the margin show a modification of the process, whereby the epiblast is temporarily

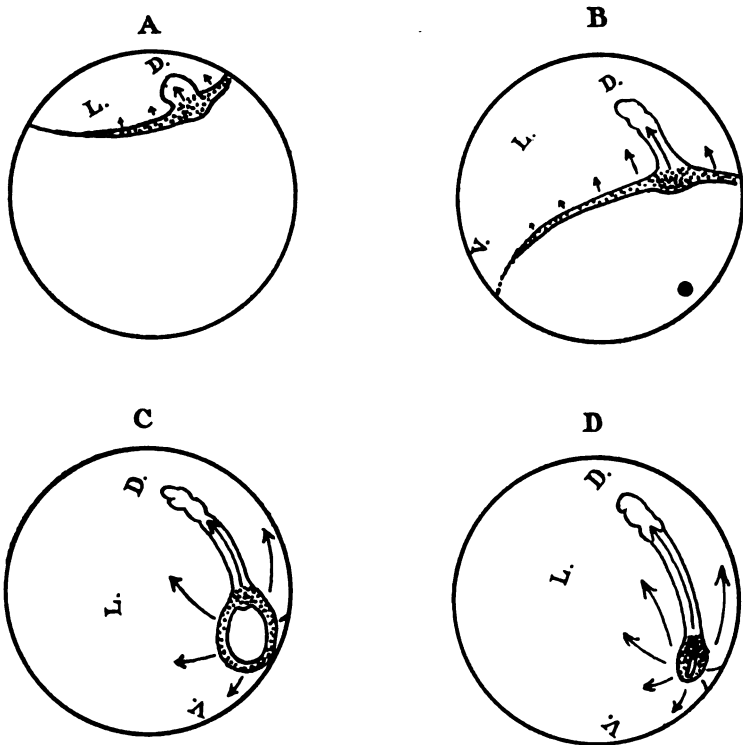


Fig. 3.—Diagrams to show the formation of the vertebrate embryo. The area v, l, d represents the "blastoderm" (in A, only d the dorsal, l the lateral parts are visible) as formed by segmentation of the egg. The dotted area is the actively proliferating secondary growth centre (lips of the blastopore), which after a while adds new material to the pre-existing parts in directions always at right angles to itself, as indicated by the arrows. The arrows also indicate roughly the extent of the subsequent blastoderm and embryo which is due to this secondary growth centre.

separated from the hypoblast, with the result apparently that it slides more rapidly over the yolk for some time, the typical blastopore lip being reformed ventrally only during the final stages of overgrowths (v. O. Hertwig (13)). It is a process which, in certain cases at least, seems to combine the method of formation of the anus of Rusconi in Amphibians in the way in which the blastopore lip is formed with the method of spreading of the blastoderm of the avine egg in its separation (though temporary) of the epiblast from the hypoblast.

The lip, as soon as formed, then adds new material to the pre-existing tissues in a direction at right angles to the edge of the rim, as indicated by the arrows in the diagram (Fig. 3), and so the growth in length is produced. This accretion is most marked in the mid-dorsal line where what is usually termed the "embryo" is laid down.

In the Teleostean, after coalescence of the rim and closure of the blastopore, the mid-dorsal part of the rim—that is to say, the part next the "embryo"—continues its activities and now grows away from the egg as the tail does in amphibians and as the Elasmobranch does from an earlier date.

The great difference in general aspect between the growth of the Elasmobranch and the growth of the Teleostean "embryo" is due to the fact that in the former the most active part of the secondary growing point is forced to lift itself away from the surface of the egg at an early time, owing to the failure of the "blastoderm edge" to keep pace in its progress over the yolk with the growth of the "embryo," as it does in the Teleost. It seems to be tied back, so to speak, at the anterior end of the gut cavity. The merocytes do not travel over the yolk at the posterior end as they do in the Teleost, and as they do at other points of the rim in Elasmobranchs. This gives to the tail end of the Elasmobranch an indented tip instead of the flat or knobbed tip of the Teleost, and a much longer delay occurs in the enclosure of the yolk.

These differences are indicated in the diagrams (Fig. 4).

The coalescence of the blastopore in Teleosteans is usually by means of a centripetal closure of a ring, but it may be, as in

Gymnarchus, that a linear streak is formed, which resembles in a remarkable manner the primitive streak of a bird and some Mammalian embryos.

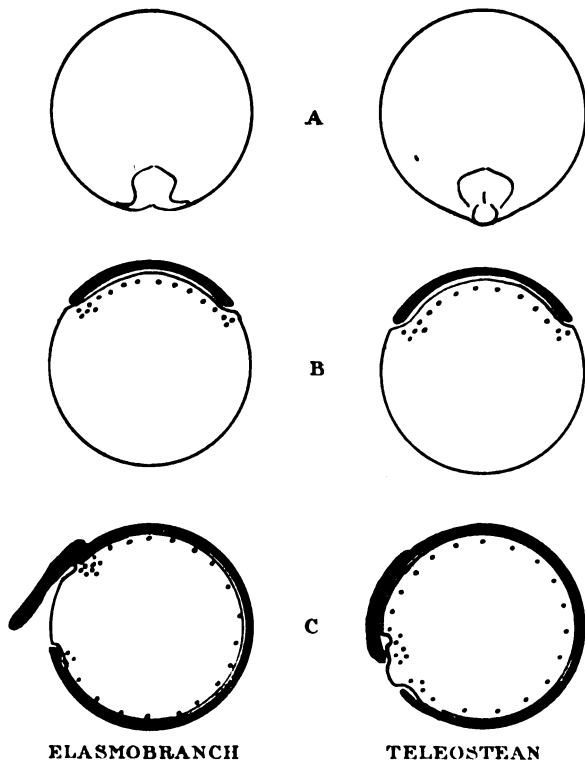


Fig. 4.—Diagrams for comparison of Elasmobranch and Teleostean embryos.

There are several peculiarities in the development of *Gymnarchus*. The egg is large. The embryo lies over on its side like a bird embryo, but not always on the same side, though more often on the right than on the left.

In the bird the embryo invariably lies upon its left side. The reason of this is, perhaps, to be found in the arching up of the anterior part of the body, owing to the cranial flexure, together with the growth outwards of the heart, as a loop to the right

side. This prevents the falling over of the embryo upon the right side, consequently it topples over to the left.

The comparison of figures of *Gymnarchus* and of a bird of corresponding age showing a primitive streak is interesting, because here we have two structures which are almost identical in appearance, which without doubt are analogous in function, and homologous in origin, and yet are brought about in totally different ways developmentally. That of *Gymnarchus* is formed by the coalescence of actual blastoderm rims, i.e., blastopore lips, that of the bird seems to be produced by expansion—that is to say, the drawing out of an area in itself circular, by reason of an internal hydrostatic pressure combined with the counteraction of two distinct agencies, the primary and secondary growth centres. It is an example of an homoplastic and homologous feature combined in one structure.

THE CONCRESCECE THEORY.

In describing the growth of the embryo and growth of the blastoderm over the yolk, it was assumed that the rim of the blastoderm is a growing point, circular in form, which adds new material at all points to pre-existing material in the direction of the arrows drawn (Fig. 3).

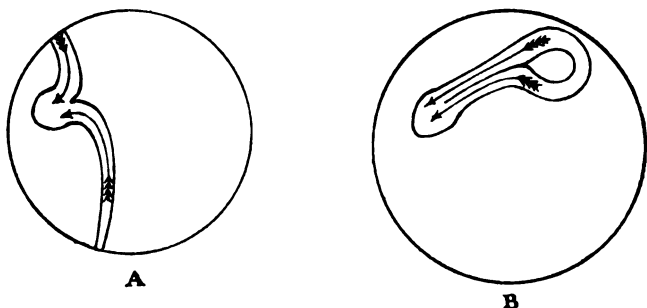


Fig. 5. -- Diagrams to illustrate the formation of the vertebrate embryo according to the concrescence theory.

(A.) Early stage, concrescence beginning.

(B.) The concrescence is nearly complete, the embryo having been formed. The blastopore may be considered as having existed along the whole length of the back.

But there is another view which is held by many, namely, that the "embryo" is formed by a *conrescence* of the rim. This theory was first formulated by His and Rabl, and is known as the Conrescence Theory.

The diagrams here given illustrate the supposed process (Fig. 5).

This theory as expressed thus, however, is not supported by experimental study. If the blastoderm rim is cut or marked at an early stage some distance away from the "embryo," no "embryo" is ever formed posterior to the mark, nor does the injury seriously affect the embryo, at least *not the dorsal organs of the future animal*.

The accompanying figures (Fig. 6) are taken from Kopsch's admirable "*Untersuchungen über Gastrulation und Embryobildung bei den Chordaten*," and represent the results of certain experiments performed by him on developing eggs of the trout.

In Fig. 6 the mark OP. represents in A the point in the rim of the disc—*i.e.*, lip of the blastopore, at which an injury was effected. Fig. 6 B shows the position of the injury at a later stage when the embryo had eight or nine pairs of protovertebræ.

According to the conrescence theory, the germinal disc rim growing round should have coalesced with the corresponding part on the other side, and formed the mid-dorsal part of the embryo, namely, neural tube, notochord, and, say, protovertebræ. But as a section B-b shows, the formation of these parts is quite normal, and the injury lies far to the side—which is, strictly speaking, in the latero-ventral—part of the future body wall. The injury has brought about a failure on the part of the rim to progress over the yolk, and a corresponding *defect at the side*—which is just what one would expect if the embryo is formed in the way described in a former paragraph, p. 353, Fig. 3.

C is a figure of a slightly more advanced embryo which had been operated upon in the same way as B. Here the operation scar certainly appears to have moved towards the mid-dorsal line. But when we come to examine sections, we find that the mid-dorsal and dorso-lateral parts of the embryo are quite

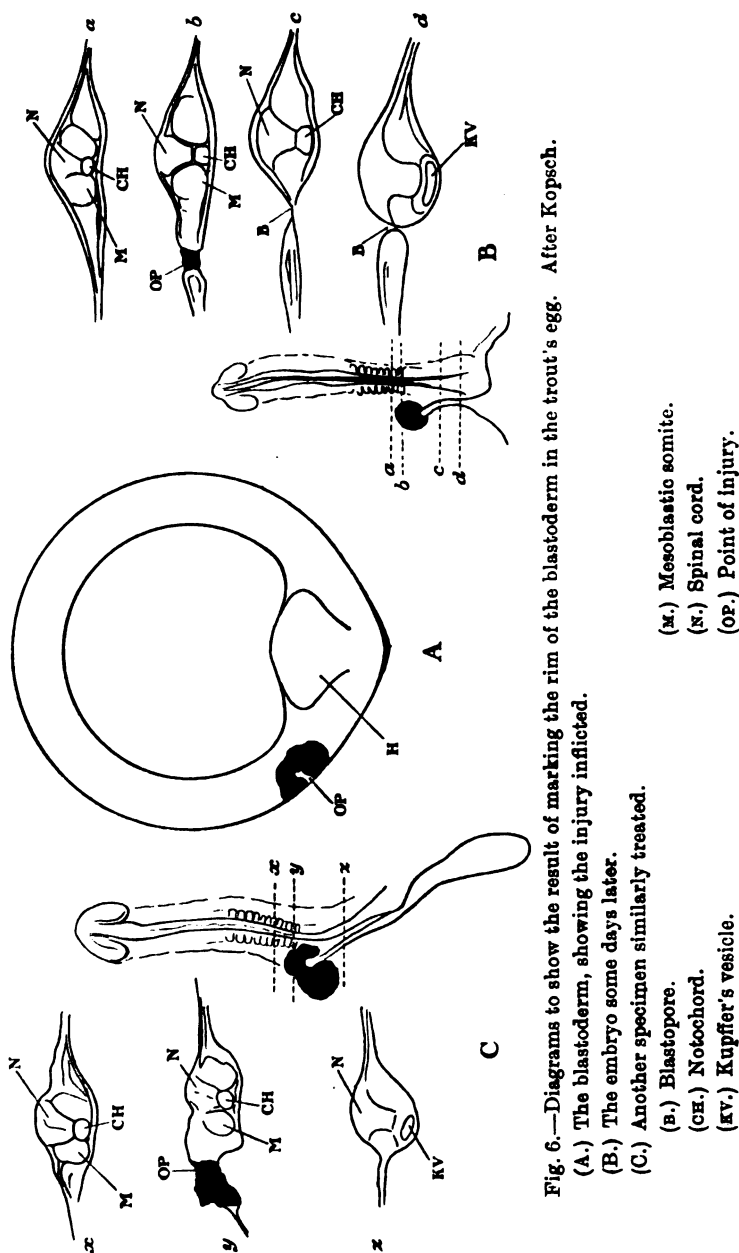


Fig. 6.—Diagrams to show the result of marking the rim of the blastoderm in the trout's egg. After Kopsch.

(A.) The blastoderm, showing the injury inflicted.

(B.) The embryo some days later.

(C.) Another specimen similarly treated.

(M.) Mesoblastic somite.

(N.) Spinal cord.

(OP.) Point of injury.

(B.) Blastopore.

(CH.) Notochord.

(KV.) Kupfer's vesicle.

unaffected. It is the part of the embryo ventral to that which will be derived from the protovertebræ which is injured.

The notochord, neural tube, and even mesoblastic somites are normally developed, but a little of the tissue beyond—that is to say, ventral to this point—is lost. This means that it is the side of the ultimate animal which will show a deficiency, which is only what one would expect upon the rival theory.

An injury made in the mid-dorsal line prevents completely any addition to the mid-dorsal region of the embryo. If the embryo were formed by concrescence this would not be so.

An injury inflicted at a point between that of Fig. A and the tail bud brings about a defect in the dorso-lateral region, leaving intact the median structures, such as the notochord and floor of the neural tube.

These experiments, to my mind, are quite conclusive against the theory of concrescence or confluence in any form, but it is only fair to say that this is not the view of all.

Even Kopsch, from whose work I have taken these figures, believes that his experiments indicate a certain amount of concrescence for the hinder end. He shows how, for instance, as in my Fig. 6C, there is a movement of the point of injury nearer to the median line, v. Kopsch (19), p. 132, Fig. 5A. It is true there is a change of position with reference to the yolk mass, but where is there any evidence that the dorsal or dorsolateral region is affected by such an injury? It is in the much distended latero-ventral region of the young embryo that the injury has been made, and it is in that region of the fully-formed embryo that the injury persists. So long as the notochord and floor of the neural tube are uninjured by such experiments as these, so long is there a complete absence of evidence for concrescence or confluence.

Furthermore, any concrescence or confluence, if it occurs, which comes short of this, loses its whole zoological interest and morphological importance.

I have dwelt at some length upon the theory of concrescence, because it is one of considerable importance from the strictly zoological point of view, apart from the question of embryonic

growth. If the formation of the mid-dorsal region of the vertebrate embryo could be proved to arise by the concrescence or apposition of the blastopore lips, then we should have strong support for the theory that the original gastrula mouth extended along the dorsal surface of the ancestral chordate, just as we believe that the original gastrula mouth extended along the mid-ventral surface of the ancestors of annelids, molluscs, and arthropods, the aperture giving rise to both mouth and anus during the evolution of those races. But if concrescence is a myth, then that evidence is non-existent, and we are led to the conclusion, derived from the fate of the actual blastopore wherever it occurs in chordata, that in the chordate phylum the original gastrula mouth became anus only, and the supposed phylitic connection between chordates and annelids or arthropods receives no support from the study of this most important phase of the developmental history.

[In dealing with embryological problems, it seems to me that where experiment is possible we ought to take the evidence derived from those experiments as more worthy of consideration than theoretical conclusions, and when a doctrine has to rely upon theory which is opposed by fact, it is time that doctrine was forgotten.

But how unwillingly this is conceded is shown by a recent writer on the concrescence theory. Sumner (25), with reference to the supposed formation of the primitive streak in birds by concrescence of the blastoderm margin as described by Duval, says, "It is true that the experiments of Assheton, 1896, have not supported Duval's theory." Then he adds, "Since writing the foregoing, I have fully confirmed such of Assheton's results as go to prove that the primitive streak of the bird does not arise from the blastoderm border in ontogeny. This in no way disproves, however, that it so arose in *phylogeny*, and I believe that there still remain strong reasons for such a view!"]

GROWTH CENTRES IN VERTEBRATE EMBRYO.

As the "blastoderm" expands and covers the yolk, much of this spreading is no doubt due to the general interstitial growth throughout the whole area and to the sliding of the ventral lip, as described before; but some of it is due to rapid proliferation of the edge or rim, which, as I endeavoured to explain last week, adds a new tissue to all pre-existing parts of the embryo.

Thus we have two parts of the embryo, the one which is due directly to the segmentation of the egg, and is prior in time to the origin of the rim, and is on the whole radially symmetrical, and the other which is due to the activity of the rim or lip of the blastopore (edge of the blastoderm), and occurs subsequent to the former, and destroys the radial symmetry by setting up a marked bilateral symmetry, and produces what is usually known as growth in length.

Can we distinguish between the parts of the future animal that have been laid down by these two agencies, which we may term primary and secondary centres of activity?

On looking at Kopsch's figures of the trout ((18) Fig. 2), we see what appears to be an anterior part, which is, so to speak, laid down upon the segmented egg, and a hinder part which is being formed by the growing edge. This is probably the correct interpretation, but as far as I know, no experiments have been made on Teleostean eggs with special reference to this point.

But two growth centres are to be distinguished in the development of other vertebrates, and in all probability they give rise to strictly corresponding parts in the adult.

In some mammalian eggs, *e.g.*, rabbit, these two centres are very clearly marked. Just before the origin of the secondary growth centre the embryo is radially symmetrical (Fig. 7). The secondary centre starts as a circular spot of rapidly-dividing cells.

This elongates and moves away from the primary centre, leaving a thick strand of tissue or trail behind it, which becomes differentiated into notochord, nerve chord, mesoblastic somites, and so on. From this figure we get a suspicion that the primary

centre provides the fore-brain, heart, fore-gut, while the secondary centre gives rise to the metamerically segmented part of the animal, the hind brain and most of the notochord. But it is impossible to test this by experiment on the mammal.

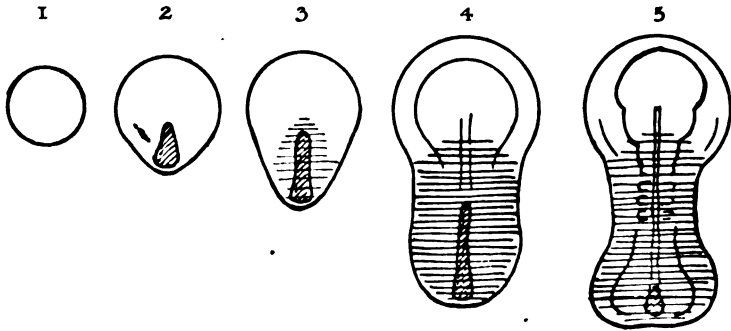


Fig. 7.—Diagrams to illustrate the appearance of the secondary growth centre and its effects on the embryonal area of the rabbit during the course of the seventh and eighth days. The white areas are those due to the activity of the primary centre, the shaded those due to the secondary centre. The doubly shaded areas are the still actively proliferating secondary growth centres known as primitive streak.

Very much the same appearance may be seen in the bird's blastoderm, and here experiment is possible.

Experiment is also possible in amphibian eggs, and in both cases the suspicion raised by the mammalian or Teleost blastoderm

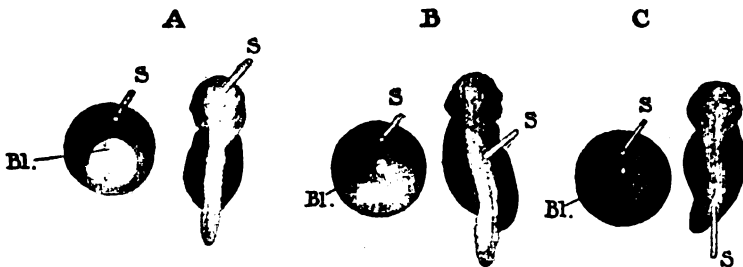


Fig. 8.—Drawings of eggs and tadpoles of *Rana temporaria* in which bristles had been inserted to determine the parts of the embryo derived from the primary and secondary growth centres. In A the bristle was inserted 5 mm. anterior to the dorsal lip of the blastopore at the first appearance. In B and C about the same distances in front of the dorsal lip, but at later periods.

is confirmed. But it is difficult to determine exactly the division between the two influences. (Fig. 8.)

It is with the hope that possibly some one might feel inclined to experiment in this direction during the next few weeks, when frogs' eggs are easily obtainable, that I show two or three slides illustrating some experiments on the eggs of that animal.

In the first experiment a bristle was inserted at the very commencement of the secondary growth centre, and appears just behind the forebrain (Fig. 8 A); in B and C a bristle was inserted in the mid-dorsal line, but it was inserted at a later period, and so appears farther back along the trunk.

Sections show that in the case of A the bristle appears at the front end of the notochord. Is, therefore, the whole of the notochord due to the secondary growth centre? Perhaps it is, but probably not; a finer method of experiment is needed. So also each organ should be tested separately.

A clear appreciation of these two growth centres aids one very much in understanding the relation of the different types of vertebrate embryos to each other.

Bearing these facts in mind, I should like you to look at the accompanying diagrams, which represent sagittal sections of Amphibian, Teleost, Elasmobranch, Avine, Reptilian and Mammalian early embryos at corresponding stages. They are shaded so as to represent the parts of the embryo derived from primary and secondary growth centres respectively.

In the Anamnia a blastopore occurs, and so the secondary centre of growth is ring-shaped. In the Amniota no blastopore occurs, though the reptilian "notochordal canal" becomes at a later period in some cases perforated, and so forms a kind of belated blastopore.

The parts due to the primary centre of growth (protogenesis) are left unshaded, though the yolk mass and primary centre endoderm are dotted where nuclei occur. The parts due to the activity of the secondary centre of growth (deuterogenesis)—the blastopore lips or their homologues—are shaded by vertical lines. Where the horizontal lines also occur the activity of the secondary

growth centre still continues, giving rise to further increase in length. (Fig. 9.)

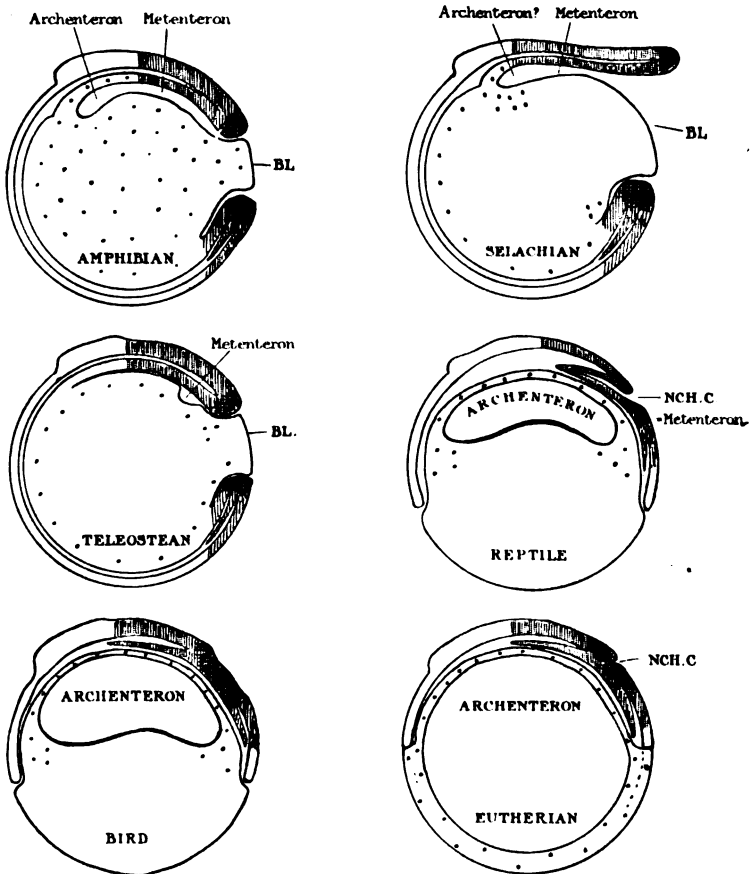


Fig. 9.—Diagrams representing sagittal sections of vertebrates at corresponding ages to show the parts of the embryo derived from the primary growth centre (protogenesis), and that from the secondary growth centre or blastopore lips (deuterogenesis). The latter, the deuterogenetic tissues are shaded. The dots represent nuclei within the yolk mass and endodermal tissues of protogenetic origin.

In the *Amphibian* embryo this centre is perforated by a blastopore which leads into a cavity, the future gut cavity of which, (a) the anterior part is wholly within the protogenetic area, and has been formed by invagination or by splitting amongst the segmentation spheres as the direct result of the protogenetic activity. This is true archenteron.

(b) The posterior part, which is roofed over by tissue which has been formed by the activity of the secondary growth centre by growth backwards of the dorsal lip of the blastopore. (This might be called metenteron to distinguish it from the true archenteron.)

The whole of the yolk mass is segmented and contains nuclei.

In the *Teleostean* the general conditions are similar to those of the amphibian, but the archenteron is temporarily obliterated, and the metenteron is present only as a small cavity, the vesicle of Kupffer. The yolk is sharply marked off from embryo and is not segmented, and contains nuclei only at the surface.

The covering layer split off together with the periblast has been omitted. It would be quite separated from the periblast by this stage.

The *Selachian* resembles the two foregoing types, but differs in the large and longer persistent blastopore and the uncertain distinction between archenteron and metenteron. There is, perhaps, a part of the gut cavity at the anterior end which is due to a modified invagination at an early stage.

The *Reptile*, *Bird*, and *Mammal* differ from the three anamnia in having large archenteron (the subgerminal cavity formed by a splitting in conjunction with infiltration of fluid), no blastopore, and, except in the case of the reptile (and, perhaps, Prototheria among mammals) a very much reduced metenteron.

In the *Reptile* the metenteron is present as the notochordal canal, which opens later by rupture of the walls into the archenteron. A similar coalescence of two cavities occurs in some other amniotes, *e.g.*, man, hedgehog, Ornithorhynchus, etc.

In *Reptile* and *Bird* the epiblast of the protogenetic area eventually encloses the yolk. In Eutherian mammals I venture to assert that it never does.

ALIMENTARY CANAL.

RELATION OF THE YOLK MASS TO THE "EMBRYO."

The next point which we should consider is the position which the great mass of yolk bears with relation to other organs in the later stages of the embryo.

The yolk mass is of course ventral, but its exact position with reference to the parts of the alimentary canal, for instance, is not the same for all vertebrates.

The position of the yolk mass in the Elasmobranch, as shown by the position of the yolk sac in the later stages, is seen to be the ventral wall of the intestine (or *bursa entiana*) just anterior to the opening of the bile duct and pancreatic duct, that is to say, it is anterior to the liver, although in the earlier stages it lies immediately posterior to the liver. In the Amniota it is in the ventral wall of the gut about the middle of the small intestine. (Fig. 10.)

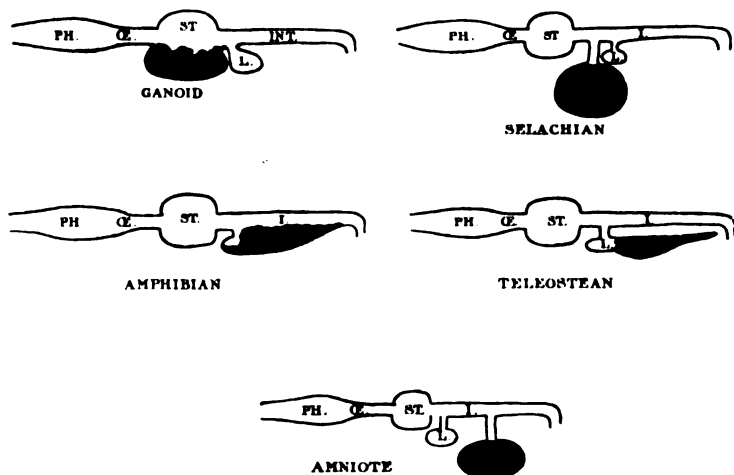


Fig. 10.—Diagrams illustrating the position of the yolk mass with reference to stomach, liver, and intestine in certain vertebrates at a late period of development.

(PH.) Pharynx.

(I.) Intestine.

(L.) Liver.

(Œ.) Esophagus.

(ST.) Stomach.

Among Ganoids, *e.g.*, sterlet, it is in the ventral wall of the stomach, but never enough to form a "sac" (Nicholas, (22)), and is at the level of the liver, but by constriction ends in being anterior to it.

In *Lepidosteus*, on the other hand, it lies just posterior to the opening of the bile duct, and like *Amphibia* and *Teleosts* is not open to the gut cavity.

In *Amphibia*, it is more difficult to locate, because the yolk is so small in amount and comparatively soon becomes absorbed, and except, perhaps, in the *Gymnophiona* it cannot be said to form a definite "yolk sac." It is posterior to the liver from the first, the liver diverticulum really being an ingrowth into it.

In the *Teleost* the yolk sac is posterior to the liver, as in *Amphibians*, and differs from both the other *meroblastic* types in that there is no connection between it and the cavity of the gut after the very earliest times, and at no time is there any possibility of yolk grains passing into the cavity of the alimentary canal.

The yolk mass may occur as a strand of yolk in the ventral mesentery running posteriorly, and separated by a mesenteric sheet; but at the anterior end the vascular system of the yolk mass clearly is in common with that of the liver, and in the latest stages the yolk mass becomes, as regards its vascular supply, a part of the liver from which it receives its sole afferent blood stream, the original supply from the gut intestine failing.

The *Teleost* is seen to be more in conformity with the *Amphibian* than other types in respect of this particular organ.

FORMATION OF HYPOBLAST AND GUT IN THE TELEOSTEAN.

The archenteron may be said to occur first as a fairly spacious cavity between the syncytium (periblast) and the other cells, as a sub-germinal cavity. As the edges of the blastopore creep over the yolk, the whole blastoderm becomes much compressed, and this cavity is obliterated and the archenteron can hardly be said to exist except potentially between the lower layer cells and the periblast.

As the blastopore narrows there does arise a distinct cavity either between the lower layer cells and periblast (*Belone*, *Coregonus*) or else within the lower layer cells (*Salmo*, etc.). This part of the gut cavity is known as Kupffer's vesicle, and in some cases is said to open to the exterior by the blastopore.

Thus Kupffer's vesicle is a part of the hind gut of the embryo, which shows a lumen from the first.

Swæen and Brachet (24) describe Kupffer's vesicle as forming posteriorly as the lip travels back, and closing anteriorly, so that it remains about the same size, and travels backwards with the progressing dorsal lip of the blastopore.

Anterior to this region there is but little, if any, lumen at first, after the suppression of the sub-germinal cavity, the hypoblast forming a sheet of tissue upon and connected to the periblast. The lumen may arise by a split occurring between the lower layer cells and the periblast, the former becoming arched up, or by a thickening of the lower layer cells into which the lumen extends subsequently. Possibly the former is characteristic of the protogenetic, the latter of the deutero-genetic regions. It would seem to be so in *Gymnarchus*.

In one way or the other a canal is formed, which soon becomes quite separated from the yolk mass except at the liver, though it remains throughout attached to it by a ventral mesentery. The notochord and mesoblast are split off from the lower layer cells long before the general gut lumen is formed.

FORMATION OF GILL CLEFTS.

The pharyngeal region is of rather special interest, for the origin of the gill filaments and their relation to the epiblast and hypoblast layers have been much discussed recently.

The mode of origin of gill clefts throughout the vertebrate series seems to be as pouchings from the gut cavity, which are necessarily lined by the hypoblast. These pouches, on reaching the epiblast, open, and causing a rupture in the epiblast, create the gill cleft. Gill filaments, to a greater or less degree, grow out from the walls of the clefts. These have been said to be hypoblastic in origin in Elasmobranchs, and I believe they are so, though Goette has (10) recently maintained that they are epiblastic.

On the other hand, the gill filaments of Amphibia have been said to be epiblastic, though all are not agreed as to this either. With reference to Teleosteans, I should like to describe the condition that exists in *Gymnarchus*, which is very interesting and suggestive.

The earliest stages I have not been able to make out, owing to insufficient material and the great distortion the embryo undergoes.

When, however, the gill clefts are nearly fully formed, the true pharynx is found to be a solid plate of hypoblast, solid as far as where the ductus pneumaticus arises. What appear to be gill clefts are not true gill clefts at all; for they are not perforations of the gut and body walls, but are depressions in the side of the head, which run together beneath—or rather internally to—the usual arches and form “branchial channels,” and are lined throughout by ectoderm. The gill filaments arise

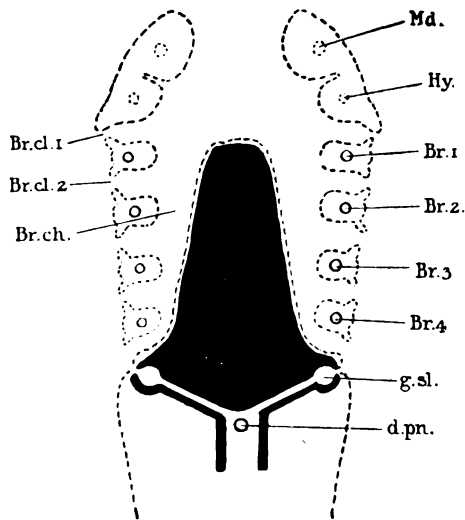


Fig. 11.—Diagram of the pharynx of a larval *Gymnarchus* showing the relation of the true gill clefts (g.sl.) to the pseudo-clefts or branchial channels. Br. cl. 1, 2, etc., branchial clefts (pseudo-clefts); Br.ch. branchial channel continuous with stomodæum; pn. d., pneumatic duct; g. sl., true gill slit; Hy. aortic vessel of hyoid arch; Md. aortic vessel of mandibular arch.

from the outer edges and are clearly epiblastic. Are we to consider these branchial clefts and channels as homologous to the real gill clefts or not?

The difference of these channels from the true gill clefts of other vertebrates is emphasized by the presence in *Gymnarchus* of one pair of real gill clefts, the hindermost. This opens to the exterior into the depression of the last branchial channel and passes as a narrow tube to the centre of the pharynx just about where the ductus pneumaticus arises. Posterior to this there is a lumen throughout. Anterior to this the lumen does not arise till later (Fig. 11).

In some Teleosteans, *e.g.*, *Cobites*, *Heterotis* or *Gymnarchus*, the gill filaments grow out to a great length, like those of Elasmobranch embryos, but they are really different, for they are undoubtedly epiblastic, while those of Elasmobranchs are almost certainly hypoblastic. The adult gill of Teleosteans is developed from the proximal ends of these epiblastic filaments, and so is epiblastic also.

The hyomandibular cleft is always partly developed in the embryo; sometimes it is open for a short time, but soon closes again. The gill clefts are covered early by the growth backwards of a fold from the hyoid arch, the operculum.

AIR-BLADDER.

Lungs or air-bladders occur in all craniate vertebrates except Elasmobranchs, and even here it has been said that a vestige may be seen.

In Teleosteans the air-bladder seldom functions as a lung, and its mode of origin is such as to lead to very important results. It develops as a single diverticulum of the wall of the œsophagus usually near the dorsal surface, and grows backwards—not into the body cavity, but above the body cavity between the peritoneum and kidney, and thus brings about a separation of the urinary from the reproductive organs. The subsequent history of the air-bladder is very different in the various families of Teleosteans. In some it disappears, in some it becomes connected with the auditory organ, in some it branches—in some it loses all connection with the alimentary canal.

The condition in *Gymnarchus* (Fig. 12) is interesting, for certainly in the larva it acts as a lung, and probably in the adult as well. In this fish it arises, as usual, as a dorsal diverticulum near to but not exactly at the middle line. Arising first vertically, it soon bends backwards and grows backwards. Almost at once it shows signs of a double condition. That is to say, it bifurcates into what we may, perhaps, call right and left lungs. The left grows backwards to the left of the median line, the right grows backwards, only very slightly, and is in reality rudimentary, except for an extraordinary anterior diverticulum which grows forwards, working its way through the solid tissue dorsal to the œsophagus. After a while it bifurcates, and the two ends swell out into little vesicles, which become closely applied to the outer wall of the sacculus of the auditory labyrinth (Fig. 12).

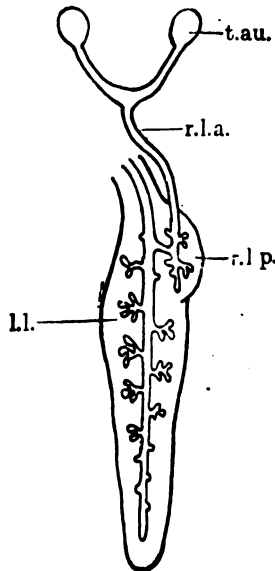


Fig. 12.—Diagram of the air bladder or lung of *Gymnarchus* of the eighth day. L.l., left lobe; r.l.a., anterior branch of right lobe; r.l.p., posterior branch of right lobe; t.au., tambour-like swelling in contact with sacculus.

In *Gymnarchus* the air-bladder is extremely lung-like in structure, being cellular, and is undoubtedly used as a lung by the larval fish, and probably under certain conditions, if not normally, by the adult. *Gymnarchus*, in several respects, shows primitive characters in its development, so that one is prompted to consider whether this lung-like condition of the air-bladder may not also be primitive, and to ask, was the *swimming bladder* derived from the *lung* by the growth of the latter along the dorsal wall of the body cavity, so that, by reason of its firm position close to the centre of gravity of the fish, it became more useful as a hydrostatic organ than as a lung?

Be that as it may, the growth of the bladder between the peritoneum and kidneys has produced one of the most marked characters of a Teleostean, namely, the complete absence of any connection between any part of the reproductive system and the kidney tubules.

LIVER, PANCREAS, ETC.

There is not much of special interest in the development of the other organs of the alimentary canal.

The tube deepens a little way posterior to the ductus pneumaticus, and from the base of this pit the liver diverticula arise. They project into the blood sinus, into which the vessels from the yolk debouch. In *Gymnarchus* this depression in the floor of the gut becomes constricted off from the rest, the more dorsal portion, and forms the gall bladder, and the actual constricted part forms the bile duct.

In the same fish the pancreas is a later development, and arises as several ducts from the walls of the bile duct, which branch and give rise to a diffuse gland lying in the omentum connecting the stomach and intestine. These glandular branches enter into close relation with some groups of cells of quite a different nature, known as the islets of Langerhans, whose origin I have not traced in *Gymnarchus*, but which are probably derived from gut epithelium, as in other forms.

About the time of the development of the liver a short dorsal diverticulum arises, which bends slightly forwards. This I believe to be the first appearance of pyloric cæca, though it shows

no double origin. This is brought down by the rapid growth of the dorsal wall of the gut just in front of it. This rapid growth gives rise to the blind sac usually known as stomach.

The accounts given of the development of the pancreas in Teleosteans are to the effect that the pancreas has three origins, one dorsal, and two ventral from the bile duct. The dorsal diverticulum is said to separate off completely from the gut. It is this so-called pancreatic dorsal rudiment which probably forms the islands of Langerhans, which are not to be regarded as forming part of the pancreas proper (Assheton (2, 3), Rennie (23)). It is a point which needs and deserves further investigation.

VASCULAR SYSTEM.

With reference to the vascular system, I do not know that there is anything which one can say is peculiarly characteristic of Teleostean development, except the circulation of the yolk sac. In the adult there is much variation in the arrangement of the blood-vessels, both of the arterial and of the venous systems; especially in connection with the organs of respiration, both gills and air-bladder, when use is made of the latter organ as a lung.

In the yolk sac circulation there is but little difference among the various members of the Teleostean fishes, but a very striking difference as compared with Elasmobranchs, after the circulation of the yolk sac has attained its highest degree of development.

In Elasmobranchs an artery (or arteries which join up to form one) passes off from the aorta (like a pronephric artery) and passes at an early stage into the yolk sac anteriorly, where it splits up into capillaries, forming an inner ring, and the blood is collected into an outer ring and passes through the umbilicus by a subintestinal vein joining the omphalomesenteric, which on development of the liver splits up into capillaries in it. The yolk sac circulation is thus arterial in the Elasmobranchs.

According to Rückert, however, this is a secondary condition. At first the arrangement is as in the Teleosteans, and is venous. Whereas in the Teleost this is retained throughout embryonic larval life, in the Elasmobranch a connection arises between the

dorsal aorta and vitelline vein, which results in a complete reversal of the circulation.

In Teleosts the yolk sac circulation is venous throughout embryonic life. The yolk sac is supplied by the subintestinal vein, and the blood after passing through the capillaries of the yolk sac is collected into a vitelline vein which gives off hepatic afferents and receives hepatic efferents, but continues as a meatus venosus into the sinus venosus.

Quite late in larval life the yolk sac loses its supply by the subintestinal vein, and receives an arterial (?) supply from the liver as mentioned before, thus behaving exactly as though it were part of the liver.

The blood-vessels are developed early upon the yolk sac before a head fold has been formed, so that the heart may appear in front of the head of the embryo, and the sinus venosus seems to lie anterior to the heart, which apparent abnormality is rectified as the head region becomes folded off from the yolk sac. The sinus venosus is formed either by two vitelline veins, or by a vena vitellina media. From this median vitelline vein hepatic afferents and efferents develop. The anterior and posterior cardinals develop as in Elasmobranchs and, joining, form the ductus Cuvieri in the usual way.

ORGANS OF EXCRETION.

I suggested as a developmental character, which might be said to be diagnostic of Teleosteans, the peculiar nature of the pronephros. The pronephros of a Teleostean at the height of its development consists of a pair of chambers, probably compartments of the body cavity, at the anterior end of the abdominal cavity, and quite shut off from it, whose walls are lined by a thin epithelium with spherical nuclei, and much invaginated by blood-vessels, which arise from and again fall into the aorta or its branches. From each of these chambers, known as the pronephric chambers, a tube, the pronephric duct, with walls formed by cubical epithelium, passes backwards, taking a more or less sinuous course till it opens to the exterior or into the extreme posterior end of the gut. The pronephric chamber has no venous

supply of blood, but the duct in its posterior length lies close alongside of the posterior cardinal sinus.

This organ occupies the position and has general characters corresponding to those of the pronephros of Amphibia, but differs in the complete separation from the rest of the coelom of the part of the coelom in which it and the glomus and nephrostome lie.

The early formation of this pronephric chamber has been carefully investigated in the case of the trout by Felix (8).

He finds that the first origin of the organ is a series of solid folds, or ridges, of which there are five in number, in the region of the third to seventh somites of the dorsal end of the lateral plates of mesoblast, including splanchnopleure and somatopleure.

These have no lumina at this stage. The ridges then coalesce, and form a single mass, which becomes divided by a fold into a dorsal and ventral portion. The dorsal part acquires a lumen and forms the anterior end of the pronephric duct, while the ventral part acquires a lumen and becomes the pronephric chamber.

In the meantime, posterior to this part, the lateral plate of mesoblast is becoming differentiated into a strand of cells, the cardinal vein and a strand which quickly acquires a lumen, the pronephric duct. This joins up with the parts developed from the folds mentioned above, and grows back caudalwards until it joins the gut at the posterior end. The dorsal portion of the original head kidney mass now comes to lie more outwardly and the ventral part medianly so as to embrace the dorsal aorta, from which a pair of loops develops, round which the pronephric chambers encroach and meet (Fig. 13 A).

Felix says both the somatopleure and splanchnopleure are involved in the formation of this organ.

Subsequently the glomus becomes larger by the development of more loops which, in *Salmo*, are said to be connected with the mesenteric artery and aorta. This constitutes the sole kidney organ of larval life, and persists for some time in the trout, being still present two years after hatching, but ultimately it disappears.

Its place is taken by the development of the mesonephros, which arises, as usual, from single cells or groups of cells lying in the mesoblast alongside of, but quite separate from, the pronephric duct. These are segmentally arranged. The groups of cells grow and become oval masses, which then develop lumina, elongate, and later break through the walls of the duct and so

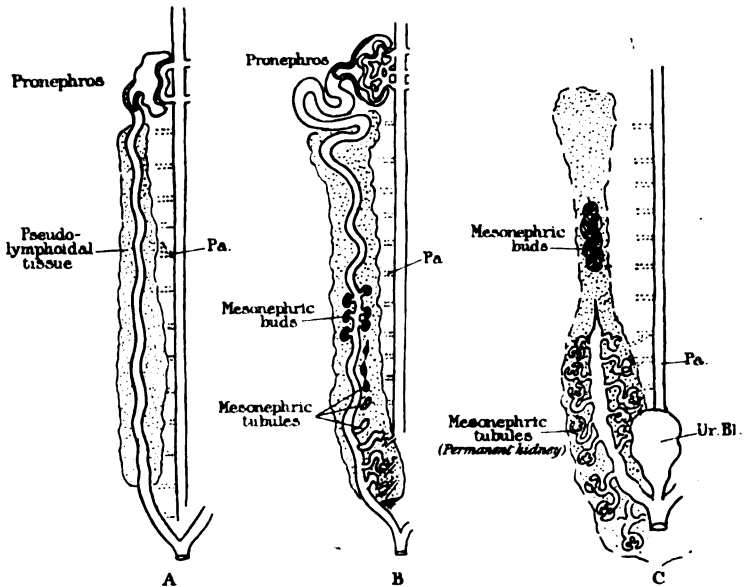


Fig. 13.—Diagrams showing three consecutive stages in the development of the renal organs of a Teleostean.

(A.) Early larval condition.

(B.) Late larval condition.

(C.) Adult.

Pa., Parietal arteries from which the renal arteries (mesonephric) arise. Ur. Bl. urinary bladder.

connection is made between the lumina. The other end develops a Malpighian body. Fig. 13, B, shows diagrammatically the development of these tubules. These tubules increase in number, secondary and tertiary ones arise, and all the tubules, together with the blood-vessels and other tissues, become the permanent kidney of the adult, thus developing after the manner of mesonephric tubules of Amphibia and Amniota, though none at any

time have nephrostomes. Some very curious problematical buds occur upon the pronephric duct among the mesonephric tubules in the anterior region, or in front of the region of the mesonephros (Fig. 13, B). These buds separate off from the pronephric duct, and their ultimate history has not been followed, although it is known that they do not give rise to kidney tubules.

The origin of the ordinary mesonephric tubules is very obscure, and possibly a cytological investigation might yield results of interest. Apparently the tubules arise from cells which seem to have no particular origin apart from the general mesoblast tissue. Sometimes they develop from single cells, at other times from groups.

In *Gymnarchus* there are some rather interesting modifications.

In the first place, the pronephros seems to be formed, more as in Amphibians and Ganoids, as folds of the somatopleure, producing funnel-shaped nephrostomes open to the general body cavity. Unfortunately, for lack of material, I have been unable to trace the separation of this part of the coelom from the general body cavity. Anyhow, the observation points to the probability of the cavity of the pronephric chamber being really general coelom, and not an expansion of the pronephric duct.

Another point of interest is that the curious buds which occur upon the pronephric duct in the anterior region of the mesonephros differ in two respects from those of *Salmo*. They are wholly in front of the mesonephric tubules, and they are accompanied by diverticula from the duct itself. These diverticula are transitory and disappear early.

At an early stage a mass of glandular-like cells appears beneath the dorsal aorta and gives rise to a lymphatic-gland-like tissue which envelopes the pronephric ducts and is honeycombed by streams of blood from the posterior cardinals. This stretches from end to end of the ducts, and remains a bulky mass anteriorly, but becomes broken up and scattered behind as the mesonephric tubules develop within it. This is called by Felix pseudo-lymphoidal tissue (Fig. 13). According to Felix, this tissue is derived from the walls of the blood-vessels, though personally I

feel doubtful about this. It seems to me to be derived from general mesoblast connective tissue.

In many Teleosteans a urinary bladder is found lying ventral to the main urinary duct, and, according to Felix, this is derived from the gut in *Salmo*.

THE REPRODUCTIVE SYSTEM.

In all Teleosteans the reproductive system is quite separated from the excretory organ, unless it be that the gonaduct opens into the extreme posterior end of the urinary duct. More often it opens separately between the anus and urinary openings.

In the majority of fishes the gonads are paired. The gonad is always continuous with its gonaduct in the male, and generally, but not always, in the female.

I will describe the course of events as they occur in *Gymnarchus*. The earliest time at which the germ cells may be detected is just after hatching. At this time the germ cells are found in the splanchnopleure of the hind end of the gut, usually lying singly among the ordinary mesoblast cells, either just beneath the peritoneum or deeper down, or in the mesentery. They do not appear to be part of the peritoneum, nor is there any trace of the thickenings of the peritoneum which occur later and form the germinal ridges. They occur irregularly on each side. A little later they appear more in the mesentery and nearer to the peritoneum and come close to the surface, but I think they are always covered by a thin layer of peritoneum. In some fishes, as in *Gymnarchus*, the gonad is single in the adult. The germ cells on the left side appear to migrate across to the right side. About this time the peritoneum begins to proliferate along a line along its dorsal wall just outside the mesentery, on each side giving rise to the germinal ridges. The one on the left, however, in *Gymnarchus*, soon disappears. Into the right one the germ cells migrate and become embedded, either singly or in groups, in the proliferations of the peritoneum. These groups are arranged quite irregularly, and there is no suggestion of a segmental arrangement. The ridge now broadens along its whole length, though anteriorly it contains no germ cells. In the latest stages that I have been able to examine the broader

ridge has begun to fold up, and posteriorly it forms a pocket which projects backwards and appears to be working its way—only a short distance has to be traversed—to the exterior, where it is about to meet a slight thickening of the epiblast and open as a separate gonaduct between the anus and ureter.

How are we to regard this gonaduct? Clearly it has at no time any connection with the pronephric duct, being separated from it by the air-bladder. It cannot be called a Mullerian duct such as that of Elasmobranch fishes.

Again, the *duct* is clearly part of the so-called germinal ridge, and so it may be regarded as an involuted portion of the gonad. It is the part of the *cœlom* which harbours the germ cells and becomes separated off from the rest of the *cœlom*. It then acquires an opening of its own to the exterior along the line of least resistance, which lies in the soft mesenchymatous tissue, between the gut and the ureter.

[I have already laid stress upon the fact that the lung or air-bladder in the Teleosteans grows back above the peritoneum, and so tends to drive the gonad away from the kidney tubules at an early stage, and it seems to me that possibly with this process has gone on the adoption of an entirely new outlet for the generative products. The gonaduct of the Teleosteans must not be regarded as a true Mullerian duct, but probably as a new structure, though, in so far as it is developed from the peritoneal lining, it may in both sexes be said to be generally homologous to the oviduct of Amphibians. I see no great difficulty in imagining that this may have come about during evolution, for the growth back of the lung between the peritoneum and the kidney tubes must have been an embryonic variation or "mutation," and would exert an unfavourable influence upon the formation of connections between the tubules and the gonad, and so have tended to encourage the formation of a new exit. Not until this new exit had been established could the air-bladder have extended the full length of the abdominal cavity, and so have attained its full value as a hydrostatic organ.]

The question of the origin of germ cells is one of great difficulty and of fundamental importance. The two chief views which are held on this matter are :—

- (a.) That the germ cells are separated off from the soma comparatively late in developmental life being derived from coelomic epithelium.
- (b.) That the germ cells separate much earlier in development, and subsequently migrate into the peritoneum.

In favour of the former view are such facts as the development of germ cells from apparently ordinary peritoneum in many animals (*e.g.*, *Sabellaria* and many Annelids). In birds and mammals also they seem to appear first in the peritoneum. On the other hand, an origin from the hypoblast or from the yolk, or even segmentation spheres, has been ascribed to them in reptiles, fishes and various invertebrates.

In Teleosts some of the germ cells undoubtedly appear to be formed somewhere else than in the peritoneum, to which they migrate later; but some authors (*e.g.*, Felix and Buhler) declare that though this is true of some of the germ cells, yet others arise later by transformation of the actual peritoneal lining cells.

THE NERVOUS SYSTEM.

In Teleosts the usual mode of origin of the central nervous system is by an axial thickening of the true epiblast, the outer covering layer remaining as a thin superficial sheet. This thickened ridge forms a keel, which ultimately becomes hollowed out to form a tube. This must be regarded as a secondary modification of the usual method of folding up of a plate, and, indeed, in some cases, a trace of such a folding may be seen, as in the pike in the head region, and in *Gymnarchus* in the middle trunk region.

It has been asserted (Calberla) that the outer layer passes inwards and lines the cavity of the tubes, but this is not true. The outer layer takes no part whatsoever in the formation of the nervous system. In this respect it shows its different nature from that of the ectodermic layer of epiblast in the Anura,

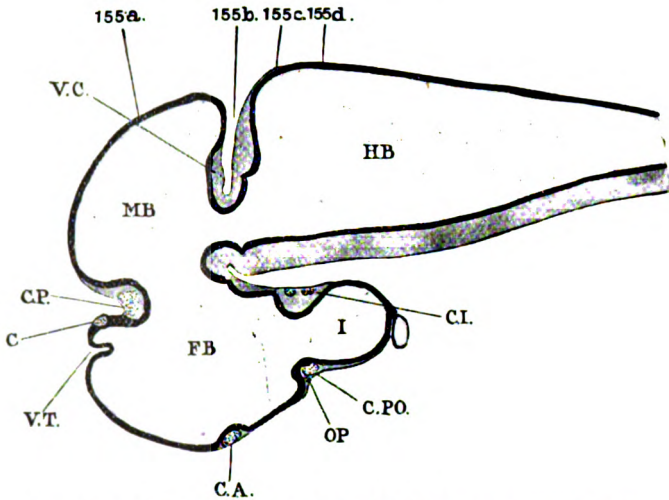


Fig 14.—Sagittal section of the brain of *Gymnarchus niloticus*.

(C.A.) Anterior commissure; C.I. Infundibular commissure.

(C.P.O.) Post-optic commissure; C.P. Posterior commissure.

(F.B.) Fore brain; H.B. Hind brain; I. Infundibulum; M.B. Mid-brain.

(O.P.) Optic nerve; v.c. Valvula cerebelli.

(V.T.) Velum transversum.

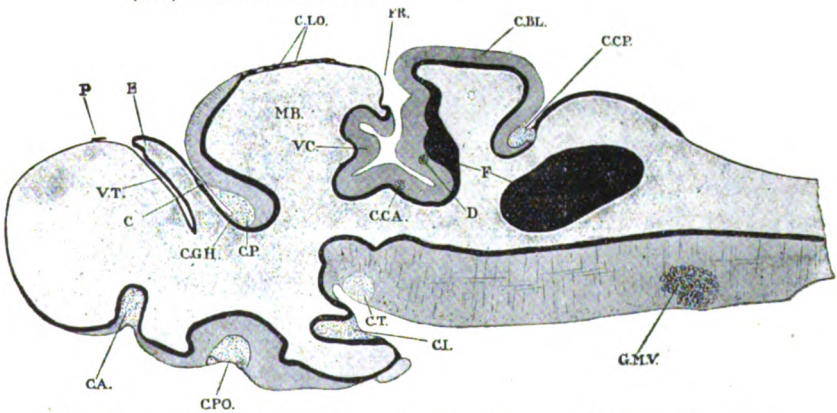


Fig. 15.—Sagittal section of the brain of *Gymnarchus niloticus* rather later.

(C.) Commissure? C.B.L. Cerebellum.

(C.C.P.) Posterior cerebellar commissure.

(C.L.O.) Commissure of optic lobes.

(D.) Commissura trachealis.

(F.R.) Fissura rhomboidalis.

(E.) Epiphysis?

(C.C.A.) Anterior cerebellar commissure.

(C.G.H.) Commissure of the ganglia trabenulæ.

(C.T.) Commissura tubercularis.

(F.) Fissure of sides of the brain.

(G.M.V.) Gigantic nerve cells.

(P.) Paraphysis?

in which case the outer or ectodermic layer is a true epiblast, and gives rise to the supporting elements of the central nervous system, the neuroglia, while the deeper or nervous layer supplies the actual neuroblast tissue.

In the same way the eye and ear arise as solid thickenings which subsequently become vesicles.

After a short time, however, the central nervous system has the usual form and is early marked out into fore-brain, and later into mid-brain and hind-brain.

A further segmentation of the primitive brain has been detected in many vertebrates, and these are specially well seen in Teleost embryos. Thus the fore-brain is further divided into two segments, the mid-brain into three and the hind-brain into six (C. Hill (15)).

A special character of the Teleostean brain is the comparatively slight cranial flexure, a difference which is very marked compared with the dogfish, and resembles more the condition of the Amphibian. A sharp bend occurs between the mid- and fore-brains, but only a slight indication of the hinder considerable flexure of the Elasmobranch occurs. (Fig. 14.)

The dorsal diverticula are far less developed than in most brains. This is specially true of the paraphysis, which, according to Kupffer, is wanting in the class. In *Gymnarchus* it is certainly present, but very rudimentary. The choroid plexus of the third ventricle arises from the simple transverse fold, the velum transversum, which separates the epiphysis from the paraphysis. This is well shown in the accompanying figure of *Gymnarchus*. (Fig. 15.)

Two features very characteristic of Teleostean adult anatomy are the failure of the cerebral hemispheres to form concavities, which is accompanied by the maintenance of a broad, thin roof to the prosencephalon, the pallium, and the development of a thick band of tissue in the roof of the mid-brain, just anterior to the cerebellum, the so-called "valvula cerebelli" (Fig. 15.) The undivided prosencephalon has the ventral wall upon each side enormously thickened, forming the corpora striata, which

thickenings bulge inwards instead of outwards, and thus no lateral ventricles are formed.

In the brain of some Anura and Dipnoi (*Lepidosiren*, Graham Kerr, 17), there is a curious upturning of the floor, which certainly seems to suggest a process by means of which the prosencephalon is divided into the two cerebral hemispheres, and the pallium thrown into folds to form a choroid plexus (Fig. 16).

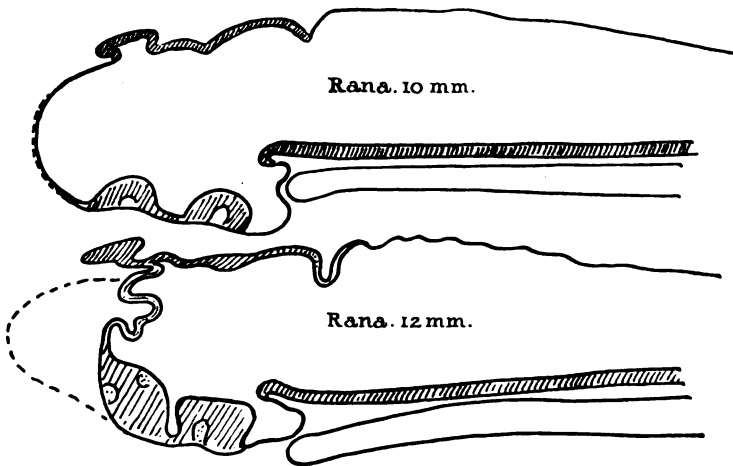


Fig. 16.—Sagittal sections of the brain of the tadpole of *Rana temporaria*, of 10 mm. and 12 mm. in length, to show how the choroid plexus of the third ventricle is formed by the upturning of the floor of the brain, whereby a comparatively thick lamina terminalis is formed.

No such upturning occurs in the Teleost, and so no thick lamina terminalis is formed.

As to the cause of the difference, I cannot say much. One might possibly arrive at it by a careful study of the development of the nerve fibre tracts and chief centres of nuclei of this region, in, say, a trout, in which there is no upturning and no cerebral hemispheres; in a frog, in which there is an upturning and hemispheres are formed; and a newt, in which there is no upturning, and yet cerebral hemispheres are formed.

The valvula cerebelli may assume very large proportions, as it does in some of the Mormyridæ. In *Gymnarchus* it is larger than usual, but is small for a Mormyrid. The accompanying figures of sagittal sections of the brain of *Gymnarchus* serve to illustrate the occurrence and position of the chief transverse fibre tracts, the paraphysis and epiphysis, the valvula cerebelli and cranial flexure, and thin lamina terminalis (Fig. 17).

Sometimes the sides of the brain coalesce in the middle line over considerable areas. Thus, in the trout this occurs in the region of the optic lobes, in *Gymnarchus* in the medulla oblongata. (F. Fig. 16.)

The sense organs do not, as a rule, show any peculiarities except as regards their origin as solid thickenings instead of foldings.

In many Teleosts the air-bladder enters into peculiar relationship with the auditory organ, as, for instance, in the "Ostariophysi," by a chain of bones developed in connection with the vertebræ.

In *Gymnarchus* the condition is very peculiar. In the side of the skull there is a large vacuity, so that the sacculus of the auditory labyrinth is widely exposed towards the exterior.

The right division of the air-bladder sends forwards a diverticulum which divides into two arms, one of which passes to the outer side of the sacculus on the right side, the other on the left. These terminal portions swell up and form vesicles, which almost, if not quite, lose their connection with the air-bladder. This vesicle lies close up against the outer wall of the sacculus, and on its other side touches a very thin plate of bone, the supra temporal, which lies close beneath the skin. This acts as a tambour, and no doubt conveys sound or vibrations of some sort from the water to the sacculus. It thus functions as the columella of an Amphibian, or chain of ossicles of a Mammal (Fig. 18).

This arrangement appears at first sight to be particularly marvellous. It is difficult to conceive how an adaptation of this kind, an association between two organs ordinarily remote from one another in development as well as in adult life, can have arisen in evolution.

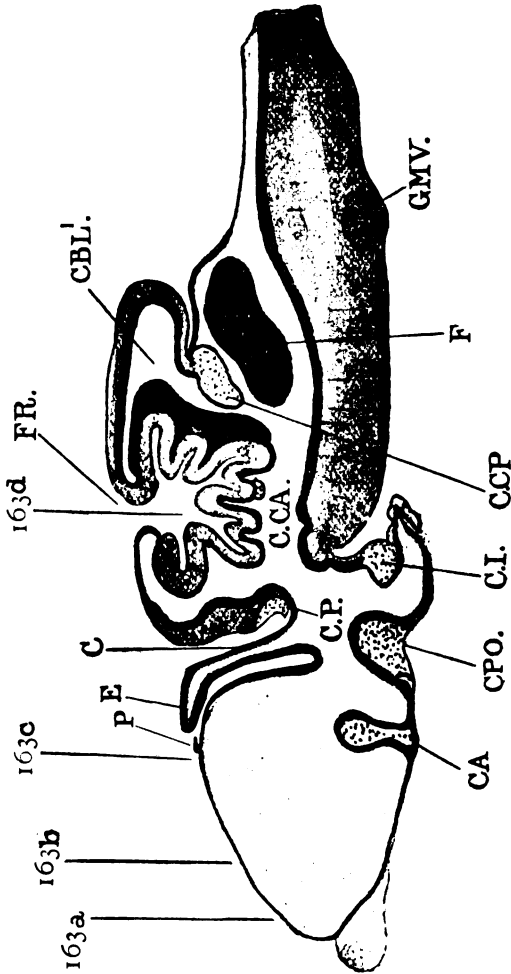


Fig. 17.—Sagittal section of the brain of *Gymnarchus niloticus*.

- | | | |
|--|--------------------|-------------------------------------|
| (c.) Commissure? | C.B.L. Cerebellum. | (d.) Commissura trachealis. |
| (c.c.a.) Anterior cerebellar commissure. | | (f.) Fissure of sides of the brain. |
| (c.c.p.) Posterior cerebellar commissure. | | (f.r.) Fissura rhomboidalis. |
| (c.g.h.) Commissure of the ganglia trabenulae. | | (g.m.v.) Gigantic nerve cells. |
| (c.l.o.) Commissure of optic lobes. | | (e.) Epiphysis? |
| (c.t.) Commissura tubercularis. | | (p.) Paraphysis? |

It points, perhaps, to a former greater diffuseness of the air-bladder. One can imagine that if an air-bladder was drawn out into diverticula—as the lungs, for instance, of a chameleon, or as

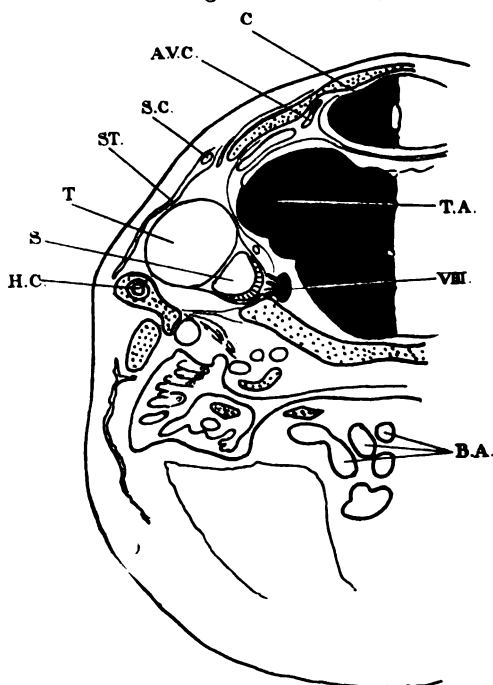


Fig. 18.—A transverse section taken through the head of a *Gymnarchus* larva of the 43rd day, showing the tambour-like arrangement of an anterior extension of the air-bladder.

(A.V.C.) Anterior vertical semicircular canal.

(C) Roof of skull.

(B.A.) Branchial afferents.

(H.C.) Horizontal semicircular canal.

(S) Sacculus.

(S.C.) Sense canal of skin.

(S.T.) Supra temporal bone.

(T.A.) Tuberculum acousticum.

(VIII.) Ganglion of auditory nerve.

it actually is in some Teleostean fishes, *e.g.*, *Corvina lobata*, *Pogonias chromis*, etc.—a diverticulum might reach the region of the auditory vesicle and there acquire a new importance.

So, although one is probably right in regarding a simple sac-like form of air-bladder as being a more primitive condition than one cut up into cæca, yet such relationships as that in *Gymnarchus* or in the *Notopteridæ* point to these fishes having passed through a phase during which they had a more incised air-bladder than at present. The function in this particular case of *Gymnarchus* would seem to be in direct connection with the perception of external vibrations, as in the ear of higher vertebrates, and to have nothing to do with the perception of pressure within the air-bladder as is usually supposed to be the case where the air-bladder is connected with the auditory labyrinth by the Weberian ossicles. For in *Gymnarchus* the connection between the tambour and air-bladder (lung) becomes obliterated.

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THE PASSAGE OF FOOD ALONG THE HUMAN ALIMENTARY CANAL.*

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UNTIL recently almost all our ideas on the subject of the passage of food along the human alimentary canal were derived from investigations performed under more or less abnormal experimental conditions in animals. But the discovery of the X-rays in 1895 was soon followed by their employment in the study of the physiology of digestion. In the next ten years our knowledge of the mechanism by which food passes down the alimentary canal was greatly extended, mainly as the result of the work done on cats by Cannon, and some time later on man by Rieder and Holzkecht.

In 1905 Cannon made some observations on himself which suggested that auscultation of the abdomen might give useful information with regard to the gastro-intestinal movements.

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Previously auscultation had been used in investigating the process of swallowing, but of no other of the movements of the alimentary canal.

The present investigations were carried out by means of skiagraphy, auscultation, percussion and palpation in normal individuals, with the object of confirming and extending the work already done, and of obtaining data to act as normal standards, with which the results of observations in pathological conditions may in the future be compared.

In this paper I shall only give an account of our own work, and shall leave the fuller consideration of its practical applications, together with the history of the subject and a review of the recent kindred investigations by others, to a future occasion.

The investigations by means of auscultation of the œsophagus and the alimentary canal were carried out in the Guy's Hospital Physiological Laboratory, with the co-operation of Messrs. F. Cook, A. N. Cox, H. Gardiner, E. G. Schlesinger and A. H. Todd. Those in which skiagraphy was employed were made in the Skiagraphic Department of Guy's Hospital, with the additional help of a number of other gentlemen; but the actual management of the X-rays was entirely in the hands of Dr. C. J. Morton, and on a few occasions of Mr. C. E. Iredell and Mr. E. W. H. Shenton, without whose aid this research could never have been accomplished.

I.—SWALLOWING.

A. *Auscultation*.—In most text-books on medicine and surgery brief reference is made to the employment of auscultation as a means of diagnosis in cases of œsophageal obstruction. But, though over thirty years ago Hamburger¹ in Austria and Allbutt² in England claimed that the method was of great value, in recent years it has been to a great extent abandoned. This is, no doubt, partly due to more reliable methods of examination which have been introduced; but probably the chief cause for the neglect of auscultation of the œsophagus lies in the want of

¹ C. W. Hamburger: *Oesterreichische medicin. Jahrbücher* xv., 133, 1868.

² T. Clifford Allbutt: *Brit. Med. Journ.*, ii., 1875, 420.

data as to what constitute the normal sounds produced by deglutition. Most physiological books are silent on the subject, and those which refer to it agree neither with each other nor with the accounts given in books on clinical medicine and diagnosis. Very little work appears to have been done on the subject since Allbutt's paper in 1875, and he gives no definite statements as to the time relations of the sounds or the effect of posture on them.

Very complete examinations have been made in the present research into the character and time relations of the sounds under various conditions in four healthy young men. In addition, several of the new facts discovered have received confirmation by a less detailed examination of a number of other individuals.

(i.) *Fluids*.—When a mouthful of water is swallowed two sounds are produced. *The first sound* is sharp and short, and is heard most loudly when the stethoscope is placed under the chin; it is somewhat less loud in the front of the neck, and can also be heard with diminishing intensity over the spine from the upper cervical down to the lumbar region, or even, in some cases, to the sacrum. In front it can sometimes be heard over the chest, but generally not over the abdomen, except in the neighbourhood of the point of maximum intensity, which is situated in the epigastrium near the left costal margin. The sound, wherever heard, occurs simultaneously with the contraction of the mylohyoid muscles and the lifting of the larynx. Hamburger,³ who first described this sound, listened to it over the dorsal spine, and believed that it was due to the passage of the fluid past the level auscultated. This view has not up to now been seriously contested, but the situation in which it can be heard and the points where it is heard loudest, as well as its time relations and the skiagraphic observations recorded later in this paper, render it untenable. The same may be said of the theory which is next most frequently adopted—that the sound is produced by the actual entry of the food into the stomach. It is much more probable that the sound is caused by the impact of the fluid against the posterior pharyngeal wall, brought about by the sudden contraction of the mylohyoid and

³ Loc. cit.

other muscles which throw the fluid from the back of the tongue across the pharynx. This explanation is borne out by the character of the sound, especially when it is heard with the stethoscope placed under the chin: it is exactly what would be produced by a volume of water coming suddenly into sharp contact with a resistant wall. Moreover, when the swallowing act is performed with the mouth empty, no sound is heard except in the neck; there it is quite faint and entirely different in character to that heard when fluids are swallowed, and is no more than the sudden contraction of the muscles could themselves produce. The sound gains in loudness with increase in the volume of fluid swallowed, until it reaches its greatest intensity with the amount which corresponds to an ordinary mouthful. If the individual is sitting or standing, the sound is louder when the head is inclined forward than backward, no doubt because in the former case a stronger contraction of the muscles concerned is required to propel the fluid in a direction against gravity, and consequently the impact of the fluid against the posterior pharyngeal wall will be more violent. Corresponding with this, the first sound is louder when the individual is in the prone than in the supine position; in the latter it is frequently inaudible, except at the neck and under the chin.

The second sound varies considerably in character and time relations according to the position of the individual examined. When he is standing or sitting it is best heard in the epigastrium and along the left costal margin near the epigastric angle. It is generally also audible, though rather less clearly, over the spine from a point varying in different individuals between the second and ninth dorsal down to the first sacral vertebra, the point of greatest intensity being generally over the spine of the tenth dorsal vertebra. It is often faintly heard over the lower part of the sternum and near the middle line of the abdomen as low as the umbilicus. When a number of observers listened over different parts of the spine and in the epigastrium simultaneously, it was found that this second sound occurred at exactly the same moment wherever it was heard, so that it would seem to be produced at one point only, from which it is transmitted in various directions.

In character, it can best be described as a trickling sound. Its average duration, which is between two and three seconds, does not depend on the amount of fluid swallowed. Moreover, when instead of a single mouthful a considerable quantity of fluid—half-a-pint for example—is drunk at once, no second sound is heard at all. The second sound begins from four to ten seconds after the first sound, which marks the initiation of the act of deglutition. Thus the normal time for the occurrence of the second sound is not the same in all individuals, so that the statement made in many text-books of medicine that if the sound be heard later than six or seven seconds after the beginning of deglutition a stricture is probably present, is quite incorrect. In no one individual was the interval found to vary more than two seconds in repeated observations. The interval is not strictly proportional to the height of the individual, although it may be noticed that the shortest interval observed, varying in seventeen records between four and six seconds, was in the smallest man examined, his height being 5 feet 5½ inches. On the other hand, the interval was identical in three individuals whose heights were respectively 5 feet 8¾ inches, 5 feet 9¾ inches, and 6 feet 3½ inches, viz., between eight and ten seconds in twenty, eight, and five observations respectively. This discrepancy disappears if the length of the legs, as measured from the anterior superior spine to the internal malleolus, is deducted from the height. Thus the man in whom the shortest interval was observed has then a measure of 2 feet 6 inches, while the three others referred to measured 2 feet 9 inches, 2 feet 9¾ inches, and 2 feet 9½ inches respectively. The interval appears to increase slightly with an increase in the amount of water drunk.

When the stomach is empty no second sound is heard until about half a pint has been drunk. The sound also disappears from the front, and shortly afterwards from behind, when the stomach is distended.⁴ In some individuals three-quarters of a

⁴ With these exceptions it is invariably heard. This is in disagreement with Martin, who says that "no sound is heard over the healthy stomach when water alone is swallowed, unless it is mixed with air." (Gibson's Text-book of Medicine, i., 644, 1901.) Moreover, no sound is heard when air is swallowed alone.

pint suffice to make the second sound disappear, but if no solids have been eaten it reappears already within a quarter of an hour, probably owing to the rapidity with which fluids leave the stomach.

In the horizontal position the second sound differs remarkably according to whether the individual lies prone or supine. In the prone position its character is identical with that of the sound heard in the vertical position. The interval between the first and second sounds is, however, almost constantly one second longer than it is in the vertical position, owing, no doubt, to the removal of the influence of gravity. The sound is absent until the stomach contains a certain quantity of material; it disappears again when the stomach becomes full, but at an earlier period than in the vertical position.

In the supine position the single trickle is replaced by a series of sounds, which are loud and best described as squirts. They are generally felt and sometimes heard by the swallower himself. The number of squirts is generally from two to five, but occasionally only one can be heard. They do not vary with the size of the mouthful. Each lasts about one second; the first of the series generally occurs three or four seconds after the first deglutition sound, and the last may begin as long as eight seconds later. The squirts can be heard even when the stomach is quite empty and when it is distended, although at these times the trickle of the vertical and prone positions is inaudible. It was found, by lying with the shoulders and legs supported, but the trunk free, that both the trickle observed in the prone position and the squirts in the supine position can be heard whether the stethoscope is placed in the epigastrium or over the tenth dorsal spine. The squirts are best heard in the epigastrium; they are also audible over the sternum, the whole of the abdomen, and the middle part of the spine.

When an individual lies on his left side, the second sound of deglutition is similar to that of the prone position; when on his right side, it is the same as in the supine position. On gradually turning round the sounds alter according to the following table, where P and S mean prone and supine, L and R left and right

lateral positions, and LP, RP, LS, and RS, the intermediate positions :—

Position.	Character of Sound.			
	Case I.	Case II.	Case III.	Case IV.
P	Trickle.	Trickle.	Trickle.	Trickle.
LP	Trickle.	Trickle.	Trickle.	Trickle.
L	Trickle, but more noisy than in P.	Trickle.	Trickle.	Trickle.
LS	Squirts, followed by faint trickle.	Trickle.	Squirts, followed by trickle.	Squirts, followed by faint trickle.
S	Squirts.	Squirts.	Squirts.	Squirts.
RS	Squirts.	Squirts.	Squirts.	Squirts.
R	Squirts.	Squirts.	Squirts, followed by faint trickle.	Squirts, followed by trickle.
RP	Single squirt, followed by definite trickle.	Single squirt, followed by definite trickle.	Trickle.	Trickle.

Thus in the position between prone and left lateral the sound is the same as prone and left lateral ; between supine and right lateral it is the same as supine and right lateral. Between left lateral and supine it is generally mixed in character ; between right lateral and prone it is generally mixed, but more like left lateral and prone than supine.

As the position is gradually changed from the vertical to the supine, a squirt sound is found to precede the trickle when an angle of about 36° with the horizontal is reached. At an angle of about 22° the trickle disappears, the normal vertical sound being now completely replaced by the supine sound. In the inverted position, with the head downwards, as a rule no second sound was heard at all. On two occasions, however, sounds somewhat similar to those characteristic of the supine position were heard.

With the body in the vertical position the œsophagus, as it enters the stomach, points downwards, forwards and towards the left. Hence in the vertical, prone and left lateral position the end of the œsophagus points downwards ; in the inverted, supine and right lateral positions it points upwards. Whatever the cause of the different sounds may be, these anatomical relations may perhaps

explain why the same sounds should be produced in the vertical, prone and left lateral positions on the one hand, and in the supine, right lateral and occasionally in the inverted positions on the other.

I believe that the two different types of second sounds—the “trickles” and the “squirts”—have not previously been distinguished. They are of some practical importance, as an observer, who was only familiar with the trickling sound heard in the vertical position, would be very likely to regard as evidence of œsophageal obstruction the squirts heard in a patient who had to be examined lying on his back in bed.⁵

(ii.) *Solids*.—The first sound of deglutition in the case of solids is identical with that already described as occurring when a swallowing movement is performed with the mouth empty. It is inaudible in the epigastrium and over the spine below the second dorsal vertebra; even in the neck and under the chin it is faint. It therefore appears to be due merely to the contractions of the muscles concerned in the first stage of deglutition.

The second sound is frequently absent in all positions. In one individual a short faint squirt-like sound, quite different from the trickle observed with fluids in character, but corresponding to it in point of time, was heard in the vertical and prone positions. Occasionally an ordinary fluid sound is heard, which is presumably due to the solid being so well mixed with saliva that it practically becomes fluid in consistency.

In the supine position as a rule there is no second sound; sometimes similar sounds to those produced by fluids are heard, probably due again to the simultaneous swallowing of saliva.

⁵ Meltzer, who speaks of a “squeezing murmur” heard near the xiphoid cartilage six to seven seconds after the commencement of the act of swallowing, as the normal deglutition sound, describes a “squirting murmur” occurring immediately after the beginning of the act of swallowing as “a trustworthy symptom of insufficiency of the cardiac orifice.” It seems probable that this is nothing else than the normal sound heard in the supine position, so that Meltzer must have diagnosed insufficiency of the cardia in all patients whom he examined when lying on their backs. For he adds that “either one or the other murmur can be heard in all but very few cases.” *Centralbl. f. d. med. Wissensch*, 1883, No. 1. Quoted without comment by Sahli (*Diagnostic Methods*, English Trans., 1906, p. 690).]

B. *Skiagraphy*.—Cannon and Moser⁶ were the first to study deglutition by the use of the X-rays, using food to which the opaque subnitrate of bismuth had been added. All their experiments were performed on animals, with the exception of a few observations made on a seven-year-old girl. She was placed in the sitting posture, and they were able to watch the rapid passage of fluid through the œsophagus, but in the lower part of the thorax it was lost to view. Solids and semi-solids were traced to a point below the heart; the motion was slow and regular, but sometimes the gelatin capsule containing the bismuth "became fixed in the upper œsophagus at about the level of the second rib. Repeated swallows of water would fail to dislodge it. . . . With each attempt at swallowing the capsule would rise slightly, as if the œsophagus was pulled up with the rise of the larynx; then the capsule would descend to its former position." These are the only published observations I have been able to find in which swallowing has been watched in normal human beings by means of the X-rays. We have observed the process in fourteen normal young men, and have found that no individual differences of importance occur.

(i.) *Fluids*.—Milk with which bismuth carbonate had been thoroughly mixed, in the proportion of about two ounces to half a pint, was swallowed. When the rays passed through the individual from side to side, the fluid was seen as a dark shadow on the fluorescent screen, passing through the thorax in the clear space between the shadows thrown by the spinal column and the heart.* In the vertical position the fluid passes with great rapidity to the back of the pharynx and thence equally quickly down the upper part of the œsophagus. A mouthful of ordinary size occupies at any given moment between one and two inches of the length of the œsophagus.

When the fluid reaches the cardia, its rapid progress is arrested owing to the sudden diminution in the lumen of the œsophagus. The lower end of the column of fluid tapers to a point which

⁶ W. B. Cannon and A. Moser: Amer. Journ. of Phys., i., 435, 1898.

* The best direction for the rays to pass in examining the œsophagus is somewhat obliquely, instead of directly from side to side—from the front of the right side to the back of the left side.

must represent the cardiac orifice of the stomach, the upper limit becoming horizontal. At a comparatively slow rate, the upper horizontal limit of the shadow descends, the lower part remaining unaltered in shape and position until the last trace of the shadow has disappeared. This means that the fluid runs through the cardia into the stomach at a comparatively slow rate, after having been shot rapidly down the greater part of the œsophagus. Hence the cardiac orifice, even during the passage of fluid into the stomach, remains very small in diameter and so offers a distinct obstacle to the onward passage of the food.

The average time which elapses between the initiation of the deglutition act and the disappearance of the last trace of fluid from the œsophagus is $5\frac{1}{2}$ seconds. It varies from $4\frac{1}{2}$ to $8\frac{1}{2}$ seconds in different individuals, and the interval may vary in one individual by as much as three seconds. About one half of the total period is required for the fluid to reach the lower end of the œsophagus, the other half being required for its passage through the cardia.

Fig. 1 represents diagrammatically the position and size of the shadow at intervals of a second during deglutition of fluid containing bismuth carbonate.

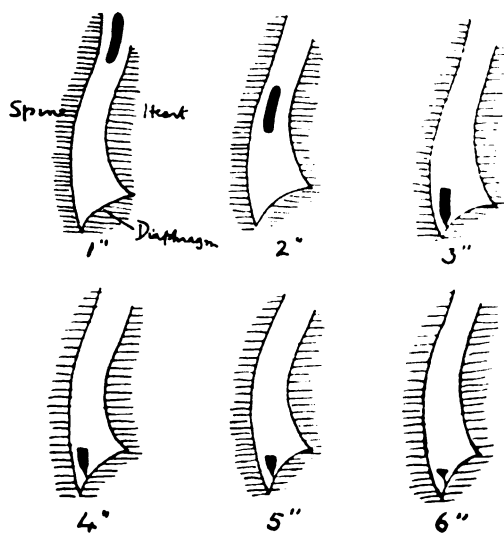


Fig. 1.—Diagram to show position of shadow at intervals of one second during the swallowing of a mouthful of milk containing bismuth carbonate.

In the horizontal position the fluid passes along the œsophagus slightly less rapidly than in the vertical position. A similar but rather more prolonged delay takes place while the fluid passes through the cardiac orifice of the stomach, the proximal end of the column being in this case rounded. Sometimes a small quantity of the fluid follows more slowly and shows on the fluorescent screen as a thin streak instead of the comparatively broad band seen when the œsophagus is filled.

In the inverted position, with the head directed downwards, the fluid can be seen steadily ascending the œsophagus at about one-third the rate it descends in the ordinary vertical position. Owing to its slower passage, the final delay at the cardia, though present, is less obvious. Sometimes a little fluid ran back from the stomach into the cardiac end of the œsophagus, whence it once again passed into the stomach.

(ii.) *Solids*.—When solids are eaten they are normally masticated and mixed with saliva until they become semi-fluid in consistency. Hence it is to be expected that their passage down the œsophagus would not differ greatly from that of fluids. A loaf of bread was baked, the flour of which had been thoroughly mixed with bismuth carbonate. When spread with butter and jam its taste could hardly be distinguished from that of ordinary bread. If properly chewed, the movement of the shadow during swallowing, whether the individual was standing or lying down, was identical in character with what has been already described in the case of fluids. There was, however, a somewhat greater tendency for small quantities to be temporarily left behind, when they were seen on the screen as a faint streak which slowly disappeared.

The passage of a solid bolus down the œsophagus is quite different. This was observed by swallowing cachets filled with bismuth carbonate. If swallowed in as dry a condition as possible, the cachet passed down the œsophagus with extreme slowness. On one occasion the cachet took fifteen minutes to reach the cardia, although the individual who had swallowed it had no sensation of its passage, and believed that it had entered the stomach when it was still high up in the œsophagus.

If a cachet was well covered by saliva in the mouth before being swallowed, or if some water was drunk immediately before so as to moisten the œsophagus, it passed down much more rapidly, the time required varying between eight and eighteen seconds. If swallowed with a mouthful of water, or if, when slowly moving down the œsophagus, some water was drunk, the solid bolus reached the stomach as rapidly as fluids.

When two or three cachets were swallowed at intervals of a second, each could be seen slowly travelling down the œsophagus. On several occasions the steady progress of one or more of the upper cachets was suddenly interrupted, and they moved a short distance upwards as if reversed peristalsis was occurring. The cause of this was probably the production of a strong contraction of the circular muscle fibres between the lowest two cachets, so that the bottom one was pushed onwards, whilst the upper ones were pushed a short distance upwards.

If the movements of deglutition were performed with the mouth empty whilst a cachet was on its way down the œsophagus, its progress was generally hastened. On a few occasions, however, the cachet was seen to ascend a short distance, as if the act had pulled the œsophagus bodily upwards. This appears to be a similar phenomenon to that observed by Cannon, and quoted above.

In the inverted position a cachet passed along the œsophagus at about the same rate as in the upright position. But when it had once reached the cardia, it appeared to have considerable difficulty in entering the stomach. Instead of continuing its forward progress, it was observed to move frequently backwards and forwards, sometimes actually disappearing, apparently into the stomach, only to reappear in the œsophagus a second or so later. On one occasion, for example, the cachet reached the cardia in twenty-three seconds, but it was not until four minutes had elapsed that it entered the stomach to reappear no more.

There is no doubt that the rapid passage along the œsophagus observed in the case of the bread corresponds much more closely to what occurs when ordinary solid food is swallowed than the

slow passage of the cachets. But the latter is of interest as indicating what probably happens when solid food is swallowed without being properly masticated. The feeling of pressure in the chest experienced after a hurried meal is thus probably due to the distension of the œsophagus caused by the presence of solid lumps of food, which only pass very slowly downwards.

C. Explanation of the second sound of deglutition.—From the character of the second sound we thought at first that it must be due to the trickling of the fluid from the œsophagus through the cardia into the stomach. But the time relations recorded above threw great doubt upon this idea. The shadow disappears from the œsophagus from $4\frac{1}{2}$ to $8\frac{1}{2}$ seconds after the commencement of swallowing; as half of this time is occupied by the passage of the fluid into the stomach, the second sound should begin from 2.3 to 4.3 seconds after the first sound, if the suggested explanation were correct. But it actually begins from four to ten seconds after the first sound, so that its commencement appears to correspond in time with the final disappearance of the fluid from the œsophagus. This was proved, in fact, to be the case on a number of occasions on which I listened to the deglutition sounds at the same time as observations were being made by means of the X-rays; it was constantly found that the sound only began *after* every trace of fluid had entered the stomach.

It is thus not easy to find an explanation for the production of the second sound. At present I can only suggest that it may possibly be associated with the fall in pressure in the bottom part of the œsophagus and the rise in pressure in the stomach when the fluid passes through the cardia; consequently gas is forced from the stomach into the œsophagus and produces the sound.

II.—THE MOVEMENTS OF THE STOMACH.

Cannon,⁷ listening over his own pylorus, heard loud, rattling, explosive sounds which recurred regularly about every twenty seconds. They were most obvious after food of a spongy nature had been taken, and when he lay down on his back or left side.

⁷ W. B. Cannon: Amer. Journ. of Phys., xiv., 339, 1905.

Though we have repeatedly tried to confirm this observation, we have almost invariably failed. On one occasion I heard sounds answering to Cannon's description which recurred five times at intervals of twenty seconds; in another individual I once heard similar sounds recur four times at intervals of eighteen seconds. More recently I have listened to the abdomens of two individuals after they had taken a frothy meal, as recommended for the purpose by Cannon. In the case of one of them I heard a series of sharp pops repeated with perfect regularity every seventeen seconds for about five minutes; in the other I could distinguish no rhythmical sounds. With these three exceptions, no rhythmical sounds were ever heard. For three or four hours after a moderately big meal, sounds can be heard over the stomach; but they are quite irregular in character and rhythm, and it seemed quite impossible to pick out from the confused jumble of sounds any one which might recur at regular intervals.

With regard to the skiagraphic examination of the stomach after food containing bismuth carbonate has been taken, we have found nothing which has not already been observed by a number of other workers. We have been able to confirm the statement first made by Rieder, that the normal position of the stomach is vertical. We are also able to confirm the account first given by Cannon as to the movements of the stomach. His observations, which were made chiefly on cats, were shown by Rieder, Holzknecht, and others, to be true also for human beings. The cardiac half of the stomach is in a condition of tone which gradually increases as the pyloric half empties itself into the duodenum. Peristaltic waves occur only in the pyloric half. They can be seen distinctly on the fluorescent screen as depressions in the edge of the shadow, travelling slowly and with increasing strength to the pylorus. The functional division of the stomach into a cardiac part, which acts mainly as a reservoir, in which salivary digestion can continue for a considerable period, and a pyloric part, which is concerned in the thorough mixing of the food with the gastric juice and the regulation of its passage into the duodenum, has also a definite anatomical basis. The

constriction which normally divides the stomach into two halves may sometimes be so well marked that it may lead to a diagnosis of an hour-glass constriction being erroneously made.

The following case, which was sent to my Out-patients by Dr. Webb, of Stoke Newington, is of interest in this connection :—

Case of duodenal ulcer with skiagraphic signs simulating an hour-glass stomach (reported by Mr. C. M. Plumptre).—Henry N., æt. 43, complained of sickness and abdominal pain after meals. He had been quite well up to five years ago, but since then he had been troubled with indigestion. At first he only occasionally had pain, perhaps once or twice a month, but lately the pain had become more frequent, occurring during the last year after every meal. During the last year he had had a great deal of sickness, and for the last six months he had been sick every day. The pain came on immediately after the patient took food, and was only relieved by sickness. It was mostly situated under the upper part of the right rectus and round the umbilicus. The patient had sometimes noticed that the vomited material was black, like coffee grounds. He had lost over a stone in weight in the last two years.

On examination, the right rectus was found to be more rigid than the left. An area of skin, about two inches broad, extending from the level of the umbilicus to the costal margin, was hyperæsthetic, the hyperæsthesia being more marked on the right than on the left side. There was deep tenderness over the same region, but nothing abnormal could be felt in the abdomen.

The length of the history without the presence of a tumour or wasting, more than what would be explained by the fact that fear of pain induced him to take very little food, made a diagnosis of cancer improbable. The area of cutaneous and deep tenderness suggested a duodenal ulcer, but the occurrence of pain immediately after food was more in favour of a gastric ulcer, as the pain of a duodenal ulcer comes on later, and is often relieved by the taking of food.

On two occasions Dr. Morton made a skiagraphic examination of the patient with me at short intervals after he had taken two ounces of bismuth carbonate in a basin of bread and milk. Immediately after the food had been swallowed a rounded shadow was seen under the left half of the diaphragm. Very quickly this became lengthened towards the umbilicus. In a quarter of an hour the shadow was seen to have definitely separated into two rounded parts, one just under the left half of the diaphragm, the other just above the umbilicus, and for the most on the right of the middle line (Fig. 2 (a)). The two parts were connected together by a narrow band, which formed a much fainter shadow than either of the rounded parts. Very

active peristaltic movements were seen in the lower division travelling from left to right. Gradually the upper division diminished in size without any corresponding change occurring in the lower division (Fig. 2 (b)). After about four hours the latter

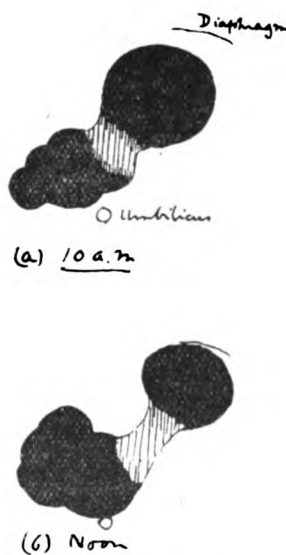


Fig. 2.—Case of duodenal ulcer simulating hour-glass stomach.
Bismuth breakfast at 9.45 a.m.

also became gradually smaller, and an hour later the former had completely disappeared. Finally the shadow of the lower division disappeared also, the complete emptying of the stomach occupying more than seven hours.⁸ The skiagraphic observations, taken with the clinical aspect of the case, seemed clearly to point to the presence of a gastric ulcer in the centre of the stomach, giving rise to an hour-glass constriction. The abnormally large size of the pyloric division of the stomach suggested that a second ulcer was present at the pylorus.

⁸ Our observations show that nearly all of a bismuth meal disappears from the stomach normally in from five to nine hours, but traces may remain much longer.

Mr. Rowlands operated on the patient and found that he had a large chronic ulcer on the upper and front surface of the first part of the duodenum. This, no doubt, gave rise reflexly to spasm of the pylorus, and so led to the dilatation of the antrum pylori. There was, however, no gastric ulcer, and the apparent bilocular condition of the organ when observed with the X-rays was due to an exaggeration of the normal constriction between the cardiac and pyloric divisions of the stomach. In confirmation of this, a circular constriction about half way between the cardia and pylorus was observed to appear and disappear again during the operation.⁹ Mr. Rowlands performed a gastro-jejunostomy, and the patient has done very well, having been free from pain since the day after the operation, which was performed nine weeks ago. On again examining the patient after a bismuth meal it was found that the stomach has now become more nearly normal in size and position, but the bilocular appearance is still obvious. The bismuth could be seen to issue, at any rate in part, out of the new opening into the jejunum.

In a number of cases we have been able to confirm the observations of Grützner and others, which show that the first part of a meal passes into the pyloric half of the stomach, whilst the later part remains in the fundus, no mixing of the contents of the two parts of the stomach occurring. Thus if some food mixed with bismuth carbonate is eaten shortly after a meal containing none of the salt, a rounded shadow just under the left half of the diaphragm is seen, whilst the pyloric portion of the stomach at first remains invisible. After some time the first part of the meal passes into the duodenum, and the food containing bismuth gradually replaces it in the pyloric part of the stomach, which therefore becomes visible. Observations of this sort show that the order in which the chief courses of a dinner are arranged is physiologically suitable, as the part containing most carbohydrates comes last, and so remains for a time in the fundus, where salivary digestion can continue, whilst the part rich in

⁹ Mr. Rowlands tells me that he has since seen exactly the same condition during an abdominal exploration in a patient with a stomach otherwise perfectly normal.

proteids passes quickly to the pyloric end of the stomach, where peptic digestion begins early and salivary digestion soon becomes impossible.

Note on the administration of bismuth salts for the skiagraphic examination of the stomach and intestines.—Until recently it was believed that bismuth salts could not be taken safely in doses larger than half a drachm or at most a drachm. This idea seems to have been handed down from the period when bismuth compounds were generally contaminated with arsenic, the poisonous action of which was erroneously ascribed to the bismuth. Rieder was the first to show that large doses of pure bismuth salts can be taken without danger. We have given bismuth carbonate in amounts varying between one and two ounces on about fifty occasions, without ever observing the smallest ill-effect, with one unimportant exception, when an individual experienced slight nausea, which only lasted a short time, after taking two ounces of the salt in milk. On no single occasion was constipation or any other disturbance in the normal activity of the alimentary canal produced, so that the time relations obtained by means of the X-rays, which are described later, can be looked upon as normal and uninfluenced by the bismuth meals. The bismuth is best taken well stirred up in a bowl of bread and milk, when it is not at all unpalatable. It may also be taken in the form of bread made from flour which has been mixed with bismuth carbonate.

Worder, Sailer, and Pancoast¹⁰ report six cases, in which alarming symptoms of poisoning were observed after two to four ounces of perfectly pure bismuth subnitrate had been given for diagnostic purposes. But the symptoms, which came on from one to four hours after the bismuth had been given, whether by mouth or rectum, were probably produced by the acid, and not by the base of the salt, as no similar accidents have occurred when the carbonate has been given, and the symptoms were quite unlike those generally produced by acute poisoning with heavy metals. The reporters of these cases suggest that some nitrite

¹⁰ Univ. of Penna., Med. Bull., xix. 131 and 137, 1906.

was formed by intestinal fermentation from the subnitrate, as the symptoms (nausea, cyanosis, prostration, full bounding and rapid pulse, fast respiration) were similar to those of nitrite poisoning.

Mr. Finnemore, the Hospital Pharmacist, has kindly investigated the question for me from the chemical standpoint. He writes: "Two grms. of bismuth subnitrate were added to 50 cc. of 0.25 per cent. HCl (to represent the gastric juice) at a temperature of 38° C. In eight minutes a portion was filtered off, and only a trace of HCl was found in the filtrate; in fifteen minutes no HCl was present. On testing the filtrate, however, it was found that HNO_3 was present, and on titration it was proved to be nearly of the same strength as the HCl originally employed. The reaction which occurs is



If insufficient HCl is present in the stomach to act on all of the very large doses of bismuth subnitrate given, the residue of the salt would be converted by the alkaline juices in the intestines into the oxycarbonate with simultaneous formation of sodium nitrate. The nitric acid would be rapidly absorbed and would circulate as sodium nitrate, and all the sodium nitrate formed in the intestines would also be absorbed. From four ounces of the subnitrate of bismuth one ounce of sodium nitrate would be formed. It has been proved that when large doses of nitrates are taken, a small proportion is excreted as nitrite. Hence it is quite conceivable that when half an ounce, or an ounce, of sodium nitrate is absorbed into the circulation, sufficient nitrite would be formed from it to give rise to serious symptoms of poisoning.

In view of the fact that two ounces of bismuth carbonate produce no constipation in normal individuals, it becomes a matter worthy of further investigation how the ten grains (one ninety-sixth part of the dose!), so often given with apparent success in cases of diarrhœa, can act.

III.—THE PASSAGE OF FOOD THROUGH THE SMALL INTESTINES.

Auscultation of the small intestines has given us no important results. In most individuals sounds of various descriptions can be heard over the small intestines at all hours of the day. They

vary greatly in intensity and in character in different people and at different times in the same person. No constant variations were discovered, although, as might be expected, the sounds were most frequent and loudest during the first few hours following each meal.

Moreover, we have constantly found that the sounds produced in the small intestines are louder when the person examined lies on his left side than when he is upright or on his back or right side. It is not easy to explain this, but it is possibly due to the anatomical relations of the mesentery and small intestines, which perhaps cause the intestinal loops to form larger curves when the individual lies on his left side than in any other position; for it is probable that gas and fluid would pass most freely through the gut when in this condition.

In spite of listening over all parts of the abdomen at all hours of the day, we were never able to hear any trace of sounds which showed accurate rhythmical variations such as those heard by Cannon¹¹ when listening to his own abdomen. He describes sounds which occurred regularly at intervals of seven or eight seconds; they were clearest in the morning before breakfast, but were also audible at other times. They were generally loudest in the left lower quadrant of the abdomen. He not only heard them, but he obtained graphic records showing their rhythmical occurrence. I am quite unable to explain our failure to confirm Cannon's remarkable observations. So far as I am aware, they have not yet been confirmed by any other investigator.

The old experimental methods, in which the intestines of an animal were exposed to view, demonstrated the occurrence of peristaltic waves, which propelled the contents of the small intestines slowly down towards the cæcum. Cannon,¹² by means of X-ray examinations in cats and dogs, discovered that another and entirely different type of movement occurred, which he termed segmentation. This probably is the normal appearance of the "swaying pendular movements," first described by Ludwig,

¹¹ W. B. Cannon: *Am. Journ. of Physiol.*, xiv., 339, 1905.

¹² W. B. Cannon, *Am. Journ. of Physiol.*, vi., 251, 1902.

which are seen in the exposed gut of animals, whose splanchnic nerves have been cut. Pfaff and Nelson,¹⁸ on the strength of sixty negative experiments, have recently denied the existence of segmentation, even in cats; this is difficult to understand, as on the only occasion on which we watched the intestinal movements in a cat, segmentation—exactly as described by Cannon—was perfectly obvious.

The shadow of the small intestines cannot, as a rule, be very definitely seen in man, owing to the rapid passage of the bismuth through them and the diminished concentration of the salt due to the large quantities of digestive juices present. This probably accounts for the fact that when we began our investigations segmentation had never been observed in man. But in three healthy individuals, and in three patients who had been given bismuth meals for diagnostic purposes, we have been fortunate enough to see the shadow of a short length of small intestine, and to watch its movements at intervals over a period of half an hour. Apparently a small quantity of food, containing more bismuth than the rest, kept together as it passed along the gut on these occasions. We were, in the first place, able to trace the onward movement of the shadow as a whole, due no doubt to ordinary peristalsis. It was obviously impossible to ascertain the rate of movement, as it occurs in such varying directions and in more than one plane.

All who were present were also able to see definite segmentation occurring. The shadow of the short length of small intestine, at first of uniform thickness, became constricted in its centre; the constriction increased until the single shadow was more or less completely divided into two. Then each half underwent a similar division, but the two central segments of the four produced by the second division joined together. The new central segment then divided again, the segmentation continuing, in one case, at the rate of ten divisions in a minute and a half. The process is shown diagrammatically in Fig. 3.

We have thus been able to demonstrate in the human small intestine the existence of peristalsis, which causes the forward

¹⁸ F. Pfaff and L. Nelson, *Journ. of the Am. Med. Assoc.*, xlvii., 1819, 1906.

movement of its contents, and of segmentation, which causes the chyme to be thoroughly mixed with the pancreatic juice, the bile and the intestinal juice, and brings every portion into frequent contact with the absorbing mucous membrane, without influencing its forward movement along the alimentary canal.

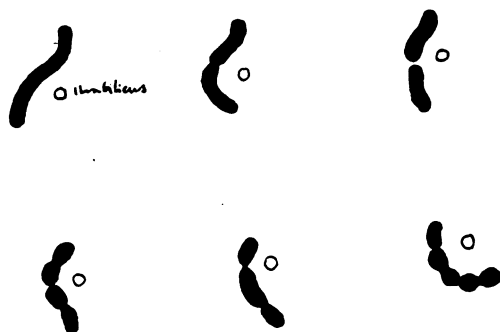


Fig. 3.—Diagram of segmentation in human small intestines occurring simultaneously with peristalsia.

IV.—THE ARRIVAL OF THE INTESTINAL CONTENTS IN THE CÆCUM.

A. *Skiagraphy*.—On eight occasions we made skiagraphic observations at short intervals on normal individuals who had taken an ordinary meal, to which one or two ounces of bismuth carbonate had been added, in order to determine how soon the first traces of the stomach contents reached the cæcum. We found that the shadow of the cæcum began to appear between $3\frac{1}{2}$ and 5 hours, with an average of $4\frac{3}{8}$ hours, after the food had been taken, and numerous other observations, less accurately carried out, were all in accord with these times. Thus the shadow of the cæcum is always obvious before that of the stomach has disappeared. Presuming, as we are probably justified in doing, that some of its contents begin to leave the stomach within half an hour of the beginning of a meal, it is clear that the average rate at which the contents of the small

intestines travel is $22\frac{1}{2}$ feet in 44 hours, or 5 feet and 7 inches per hour, which is equivalent to about one inch per minute.

B. *Auscultation*.—Cannon hoped to obtain evidence of the occurrence of antiperistalsis in the colon by auscultation, but he came to the conclusion that the sounds often heard in the ascending colon were due to the oscillating contractions of the walls of the sacculi described by Elliott and Barclay Smith.

It occurred to me that the sounds heard over the cæcum would more probably be due to the entry of the fluid contents of the ileum through the ileo-cæcal valve. In order to test this view we listened on a number of occasions, at short intervals throughout the day, to the sounds heard when the stethoscope was placed over the cæcum of normal individuals. Before deciding that any series of sounds originated in the cæcum we listened to other parts of the abdomen, in order to determine whether anything similar in character and rhythm could be heard elsewhere.

In the morning before breakfast, about 12 hours after the last meal had been eaten, no sounds could ever be heard over the cæcum. The silence continued until between 4 and $4\frac{1}{2}$ hours after breakfast, when a few sounds could be heard, which were quite distinct from anything present in other parts of the abdomen. The sounds gradually became louder and more frequent, until they reached a maximum in 1 hour to $2\frac{1}{2}$ hours after their commencement. After this it is not of much use to listen again to the cæcum, as the relation of the sounds to the time at which breakfast was taken is confused by the taking of other meals.

An ounce and a half of bismuth carbonate were taken with the breakfast on one occasion by four of the five individuals investigated. It was found that the appearance of a shadow in the cæcum, when examined by the X-rays, coincided in point of time with the occurrence of the earliest sounds in the right iliac fossa. In those investigations in which auscultation was practised without skiagraphy, the first cæcal sounds were always heard at about the time that X-ray observations had previously shown that the first traces of the food would reach the cæcum.

Hence it seems clear that in auscultation we have a means by which we can time the rate at which the contents of the small intestine pass from the stomach to the cæcum. Auscultation may thus take the place of skiagraphy, when the latter cannot for some reason be used, in the diagnosis of the rare cases in which constipation is due in part to the slow passage of food through the small intestines.*

The sounds heard over the cæcum are in all probability due to the actual entry of the fluid contents of the ileum into the gas-containing cæcum. Their loudness varies considerably in different individuals. When at a later period the gas is largely replaced by faecal material the sounds diminish in intensity and become less continuous. At all times they are louder in the upright than in the horizontal position, but for the first quarter or half minute after lying down the sounds are generally loud and almost continuous, owing probably to the movements of the fluid contents produced by the action of gravity.

C. *Percussion*.—It would seem probable that the resonant note heard on percussion over the empty cæcum would be replaced by a dull note when the contents of the small intestines enter it. We found in all the five cases which we examined by percussion that this does actually occur. Between one and two hours after the sounds indicating the earliest arrival of material into the cæcum are heard, the resonant note previously present over the cæcum is replaced by a dull note which spreads from below upwards, if the individual is examined in the upright position.

At first, the dull note disappears entirely when the supine position is assumed, as the contents are fluid, and will therefore spread along the posterior wall of the ascending colon when the individual lies down. The influence of posture was well shown in the case of a normal man who was examined in a number of different positions. Five and a half hours after a big breakfast had been eaten the bottom inch and a half of the cæcum and ascending colon were dull when he stood up; when he reclined

* So far as my observations go at present, I have only observed a delay in the passage of faeces through the small intestines in cases of constipation due to lead poisoning.

at an angle of 45° to the horizontal, the lowest three-quarters of an inch, and at an angle of 30° only about the lowest half inch remained dull; in the supine position there was no dullness at all.

Two or three hours after the first appearance of dullness its upper border alters only slightly or not at all on lying down. This must be due to the absorption of water causing the contents to assume a semi-solid consistency.

These results were obtained by auscultatory percussion, as well as by ordinary percussion, and were confirmed by two independent and expert observers, who were not at the time aware of the results expected, so that the personal factor was eliminated.

The investigation of the condition of the cæcum by percussion is of less practical importance than by auscultation, as it gives no definite information as to the time taken in the passage of material from the stomach to the cæcum. But should these observations be confirmed, they would show that the cæcal contents are at first fluid, and tend to collect in the cæcum so long as the upright position is maintained, and that at a rather later period they become semi-solid owing to absorption of water.

D. Palpation.—The few systematic observations we have so far made tend to show that the gradual filling of the cæcum and ascending colon can be observed by palpation as well as by auscultation and percussion, and perhaps even that the change of consistency of the contents can be traced. At any rate, they show, as the examination of the cæcum by the other means described do also, the futility of palpating the cæcum and colon, as is so often done, without taking into consideration the period which has elapsed since the last meal was taken, and also, as will be further explained when defæcation is discussed, the importance of noting when the bowels were last opened.

The accompanying table is an example of the records of observations made by different methods on the condition of the cæcum during the course of one day in one individual.

Table recording the observations on the condition of the cæcum made by different methods in the course of a day
on one individual.

Time.	Meals.	Number of hours after breakfast.	Sounds heard over Cæcum.	Percussion.	Palpation.	X-rays.
8 a.m.	Breakfast with an ounce and a half of bismuth carbonate					
9.30 ~		1½	None, except a few crackles in first half minute after lying down.	Resonant from Poupart's ligament up to costal margin.	Palpable cæcum, but feels empty.	
9.45 ~		1¾	Same as 9.30. [Nothing heard (3)] *			
10 ~		2	[Nothing heard (2)] *			
10.30 ~		2¼	Same as 9.30.			
11 ~		3	Same as 9.30	No shadow in cæcum.
11.25 ~		3½	Same as 9.30. [11.30, nothing heard (2); 11.35, nothing heard (3)].	Same as 9.30.	
12 noon		4	Few sounds, distinct from small intestines; increased for half a minute after lying, then disappear. No rhythm.		
12.30 p.m.		4½		
1.0 ~		5	Sounds increasing. [Obvious sounds, increased at first on lying, then diminished (3)].	Dull nearly up to level of anterior superior spine on standing; no dullness on lying down.	Feels fuller.	Very faint shadow in cæcum.
1.5 ~		5¾	[Definite, but not very loud or continuous, changing as at 1 p.m. with posture, (2) and (3)].			

Table recording the observations on the condition of the cæcum made by different methods in the course of a day
on one individual—continued.

Time.	Meals.	Number of hours after breakfast.	Sounds heard over Cæcum.	Percussion.	Palpation.	X-rays.
1.15 p.m.	Lunch.	5½	[Loud, almost continuous, bubbling sounds, slightly increased for half a minute on lying, then much diminished. Increased again on standing (3)]. [Same as at 1.5 p.m. (2)]. Sounds as at 1 p.m.	Dull nearly up to umbilicus; resonant on lying down. Dullness up to level of umbilicus on standing; only slightly lower on lying down.	Still fuller.	Ascending colon and faint transverse colon.
1.50 "		5¾				
2.10 "		6½	More continuous, but not louder.	Dullness up to level of umbilicus on standing; only slightly lower on lying down.
2.30 "		6¾				
3.30 "		7½				
3.45 "		7¾				
3.50 "		7¾	Sounds still present, but much less than at 3.30.			
4.30 "		8½	No sounds.			

* Notes within square brackets are of observations made on two other days—(2) and (3)—on the same individual, who had taken his breakfast at the same hour. They show the constancy of the time relations in the same individual if the conditions are unaltered.

V.—THE PASSAGE OF THE INTESTINAL CONTENTS FROM THE
CÆCUM TO THE RECTUM.

In sixteen normal individuals we have made X-ray examinations at various intervals after a bismuth meal, in some cases as often as four times on the first day, as well as once or more on subsequent days if necessary. It has already been stated that the shadow of the cæcum appears on an average in $4\frac{3}{8}$ hours after the meal has been eaten.

Between five and eight hours after the meal the hepatic flexure is reached; in from seven to ten hours the splenic flexure is reached, so that about two hours are required for the passage of both the ascending colon and the transverse colon. The average times taken are $4\frac{3}{8}$ hours to the cæcum, $6\frac{1}{4}$ hours to the hepatic flexure, 8 hours to the middle of the transverse colon, and 9 hours to the splenic flexure.

After a bismuth breakfast the shadow rarely reaches beyond the splenic flexure by four or five o'clock in the afternoon. On one occasion, however, the iliac crest was reached in eight hours, and on another the end of the iliac colon in nine hours.

If the bowels are not opened before the skiagraphic examination at 10 a.m., the remains of a bismuth breakfast of the previous day are found to have reached some point between the iliac crest and the rectum.

Fig. 4 shows the average time at which various points of the colon are reached if a bismuth breakfast is taken at 8 a.m. It does not, however, give much information as to the rate at which the last part of the colon is traversed, as after arriving at a certain point, which depends on the amount of fæces already present in the colon, the contents make no further progress until the bowels are opened. But on the somewhat unusual occasions on which part of the colon below the splenic flexure still contains bismuth after defæcation, the rate of progress through the pelvic colon can be measured. Thus on two occasions the bismuth was found to pass from the junction of the iliac colon with the pelvic colon to the junction of the latter with the rectum in six hours.

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The movements of the colon appear to be considerably more sluggish during the night than the day. Thus in the same individual, in whom only eight hours were required for bismuth

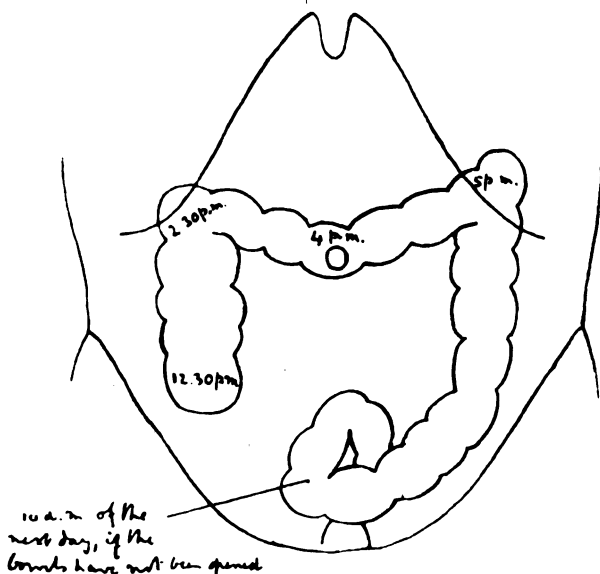


FIG. 4.—Average time at which various points of the colon are reached after a bismuth breakfast taken at 8 a.m.

taken at breakfast to reach the end of the descending colon, bismuth taken at 10.30 p.m. had only reached the hepatic flexure by 10.30 the following morning.

When the shadow of the cæcum first becomes visible, four and a half hours after a meal, that of the stomach can almost always be still seen. The remnant of food in the stomach at this period will probably also take about four and a half hours to reach the cæcum, so that it will be at least nine hours after a meal has been taken before the last traces of the products of its digestion pass through the ileo-cæcal valve. In nine hours the splenic flexure is generally reached by the material which first arrived in the colon, so that it is not surprising that the shadows of the cæcum, ascending colon, and transverse colon are normally still visible when that of the splenic flexure is first seen. By the time the

descending colon is filled, the cæcum and ascending colon, and occasionally half of the transverse colon, though generally unaltered, may be seen only as a comparatively faint shadow. But when the iliac colon is reached, the ascending colon, and half or all the transverse colon, are, as a rule, no longer seen, though frequently a faint shadow still marks the cæcum, which finally disappears when the end of the pelvic colon has been passed.

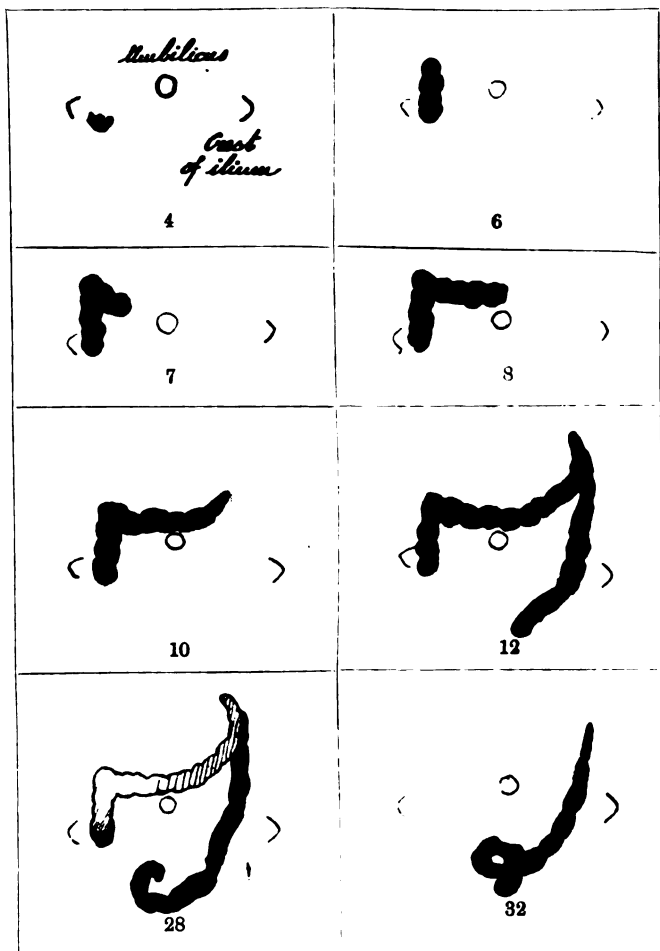


FIG. 5.—Series of colon skiagrams in a normal individual. The numbers represent the hours after a bismuth breakfast was taken.

Fig. 5 is reproduced from actual tracings made on the fluorescent screen at various periods after a bismuth breakfast had been eaten by a normal individual.

NOTES ON THE ANATOMY OF THE INTESTINES. *The small intestines.*—Too little can be seen of the small intestines by the bismuth method for much information to be derived concerning its anatomy. But one point of some importance has been very frequently observed: the last part of the ileum seems to be always situated in the right half of the pelvis, and on a few occasions the last few inches of the ileum have been actually seen rising from the cavity of the true pelvis to end in the cæcum. This is well shown in Fig. 6, the reproduction of a beautiful skiagram taken for me by Dr. Alfred C. Jordan.



FIG. 6.—Drawing from skiagram by Dr. Alfred C. Jordan, showing end of ileum issuing from the true pelvis to join the cæcum.

The cæcum.—In two healthy young men, whose bowels acted daily with perfect regularity, and whose abdominal muscles were strong, the cæcum was found to be abnormally low (Fig. 7 (a) and (b)); in both the lower part of the ascending colon was bent, with the concavity directed inwards, the cæcum being apparently situated just within the true pelvis, and in one (b) there was a second bend, the cæcum itself pointing downwards, apparently over the pelvic brim. This is of interest, as some

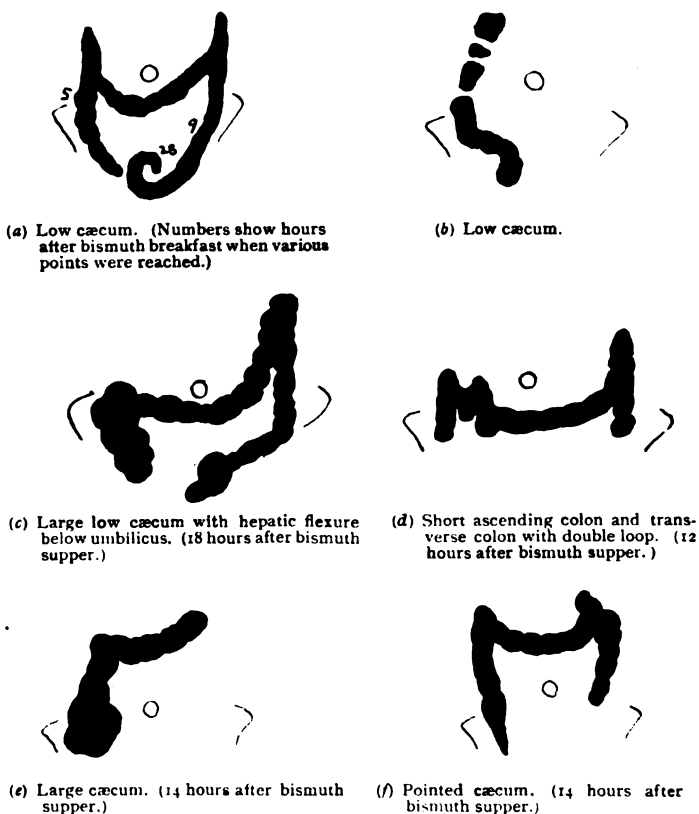


FIG. 7.—Colons of normal individuals showing anatomical peculiarities.

surgeons teach that a low cæcum is always secondary to chronic constipation.

The size of the cæcum varies considerably in different individuals. In Fig. 7 (e) and (f) the extremes which may be met with in normal adults are shown. One (e) is reproduced from a tracing of the shadow of a cæcum, the large size of which was confirmed by palpation and percussion; it is also remarkable that the sounds heard over this cæcum were louder than those heard over the cæcum of any other individual. The other figure (f) was reproduced from a tracing made at the same interval after the

bismuth meal as in (e); the unusually small size and pointed shape suggest that the cæcum was in this case rudimentary and of a similar type to that found at birth.

Transverse colon.—It is generally stated that the transverse colon normally lies above the umbilicus. We found, however, that in six out of fourteen healthy young men the transverse colon was situated above the level of the umbilicus; in one its lowest point was directly behind the umbilicus, and in seven it was below the umbilicus.

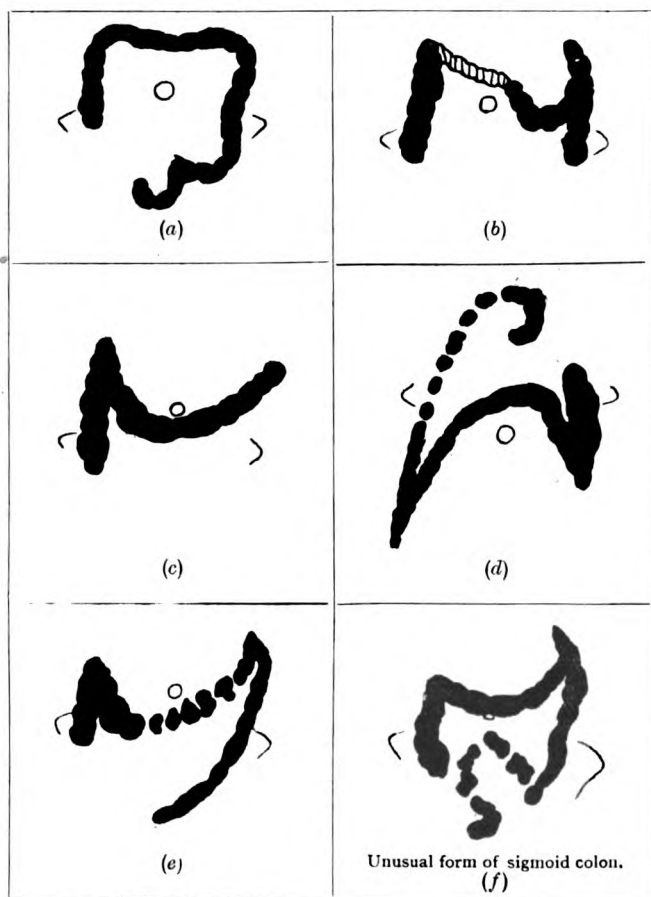


FIG. 8.—Types of normal colons.

In Fig. 8, six normal colons are shown, three with the transverse colon above, and three with it below the umbilicus.

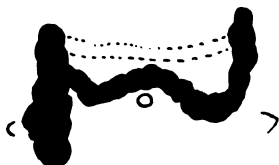


FIG. 9.—To show rise of transverse colon with emptying of stomach. Shadow of colon 11 hours after bismuth supper and 2 hours after last meal. Dotted outline shows colon four hours later, no food having been taken in the interval.

Fig. 9 shows how the transverse colon rises as the stomach empties. In another case its centre was situated just below the umbilicus an hour after breakfast, but over an inch above the umbilicus two hours later.

The movements of the colon on deep respiration will be referred to in the section on defæcation.

Flexures of colon.—The splenic flexure is usually distinctly higher than the hepatic flexure, and its position does not seem to vary much in different individuals. But the hepatic flexure is not infrequently found a good deal lower than what is generally considered to be the normal position. In one healthy individual (Fig. 7 (d)) it was below the level of the umbilicus, and the transverse colon formed a double loop, an additional flexure situated to the right of the middle line being present between the two loops. I have seen the same condition in an exaggerated degree in a severe case of chronic constipation. Both the hepatic and the splenic flexures frequently form a very acute angle, the part formed by the transverse colon being situated directly in front of that formed by the ascending colon and by the descending colon, so that the two limbs of the flexure form a single shadow when viewed with the X-rays directed from behind forwards. Examples of this are seen in Fig. 8 (b) and Fig. 10.

Fig. 8 (f) shows an unusual form of the sigmoid flexure, in which there is an acute angle at the end of the iliac colon, and consequently the ordinary loop is not present.

VI.—DEFÆCATION.

A good deal of work has been done on the nervous control of defæcation in animals, but very little is known about the actual process as it occurs in normal human beings. The only observation made under physiological conditions appears to be one of Cannon's, who watched the process by means of the X-rays in a cat, which had been previously given food mixed with bismuth.¹⁴

If bismuth carbonate is given with the food two or three times during the course of a day instead of on one occasion only, the shadow of the whole colon can generally be seen with the X-rays the next day. We have once watched the changes in the shadow which occurred during defæcation in a healthy individual prepared in this way. On six other occasions we have made tracings of the shadow immediately before and immediately after defæcation in order to find out how much of the colon takes part in the process.

Defæcation is normally started by the voluntary contraction of the abdominal muscles and the diaphragm. Owing to the simultaneous closure of the glottis, this leads to the production of greatly increased abdominal pressure. It is remarkable that in most physiological text-books no mention is made of the contraction of the diaphragm, which appears to be of even greater importance than that of the abdominal muscles in producing the rise of intra-abdominal pressure. By means of the X-rays we were able to see the diaphragm move down to the lowest position it could possibly attain, where it remained with slight variations during the straining which resulted in defæcation. The lower border of the cæcum descended about half an inch, but the hepatic flexure was depressed to exactly the same extent as the diaphragm, and almost reached the level of the umbilicus, so that the ascending colon was compressed to an almost globular form. The transverse colon descended from one inch above to one inch below the umbilicus. The splenic flexure was depressed to the same extent as the hepatic flexure, but owing to the

¹⁴ *Am. Journ. of Phys.*, vi., 269, 1902.

junction of the descending colon with the iliac colon being more mobile than the cæcum, it could be more depressed, so that the descending colon did not assume such a broad shape as the ascending colon. Fig. 10 (a) is a reproduction of a tracing taken

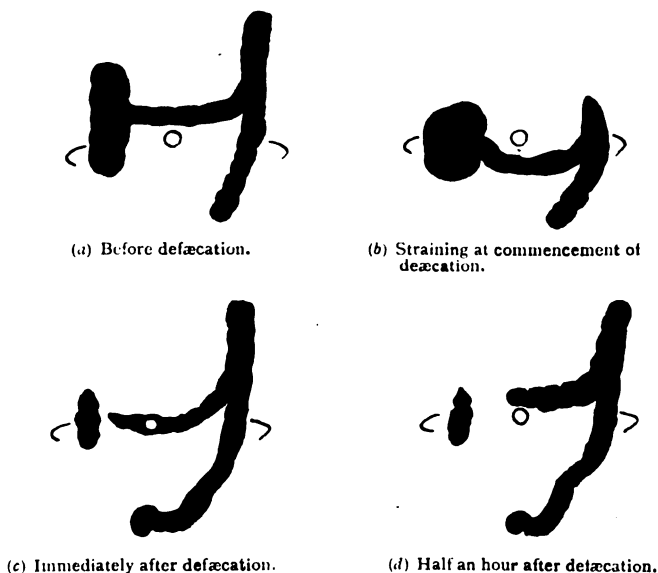


FIG. 10.—Normal defæcation.

of the colon immediately before defæcation, and (b) is reproduced from a tracing made during the act. After the straining ceases the ascending and descending colon rapidly return to their normal position, but the transverse colon rises very slowly, and may not return to its former height for over an hour. This is seen in (c) and (d) of Fig. 10, and also in Fig. 11.

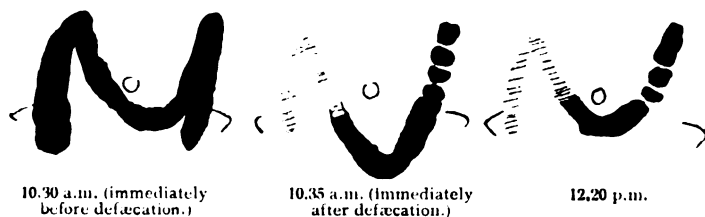


FIG. 11.—Normal Defæcation.

It is often stated that "in healthy individuals, except just before defæcation, the rectum is empty, and the pressure of fæces in this part of the bowel at once gives rise to discomfort, and to a desire to defæcate." This is not strictly accurate, as when a rectal examination is made on a normal individual, whatever interval may have elapsed since the last defæcation occurred, the rectum is found to contain more or less fæces. It is quite exceptional to find the rectum empty. It is probable that the desire to defæcate is felt only when the rectum is to some extent distended with fæces.

The increased intra-abdominal pressure produced by the contraction of the diaphragm and abdominal muscles will cause fæces in the pelvic colon to move towards the anus, which is the direction of least resistance. Thus the rectum will become more distended, and fæces will be forced into the anal canal, which is normally quite empty. Both the distension of the rectum and the irritation of the mucous membrane of the anal canal by fæces give rise to afferent nervous impulses, which produce the reflex act required to complete the defæcation. This is generally described as consisting of "strong peristaltic contractions, which take place along the whole of the descending colon, sigmoid flexure, and rectum, while both sphincters are relaxed." But our observations lead to the conclusion that the cæcum, ascending colon and transverse colon are also active in defæcation. Thus on the occasion on which we watched the actual process of defæcation, active peristaltic contractions appeared to occur in the cæcum and ascending colon. But much more conclusive evidence was obtained by comparing the tracings obtained immediately before and immediately after defæcation. The shadow of the cæcum, ascending colon and a small part of the transverse colon generally become thinner and much fainter; this must be due to the peristaltic contraction of their walls, causing their contents to pass further along the colon.

This is seen in the tracings of two cases reproduced in Figs. 10 and 11. In another case the activity of the ascending colon was shown in a different way. At 9 a.m. the individual concerned felt, as usual, the desire to defæcate, but as he had on the

previous day taken a bismuth supper, he wished to give us the opportunity in the evening of examining his colon before and after defæcation. He therefore restrained the desire. The desire to defæcate, at one time almost irresistible, soon disappeared, but on examination at 10 a.m. no shadow was seen in any of the colon, except in the iliac and pelvic parts, the latter being much distended. This suggested that the violent desire to defæcate at 9 a.m. had resulted in the whole of the first part of the colon emptying itself into the distal part. Another half-ounce of bismuth was taken at noon. At 8 p.m. this had reached the hepatic flexure, so that the cæcum and ascending colon could be seen, as well as the iliac colon and pelvic colon (Fig. 12, *a*). After defæcation, some minutes later, the distended pelvic colon was found to have rid itself of the excess of fæces it contained. The cæcum and ascending colon had partly emptied their contents into the transverse colon, the first part of which was now visible (Fig. 12, *b*). The descending colon, previously containing no bismuth, could now be clearly seen. The source of its new contents is not obvious, as the greater part of the transverse colon was still invisible. Possibly it came from the transverse colon, where it may previously have been too diffused to make a definite shadow: less probably it came from the pelvic colon by a process of retroperistalsis.

In most cases the shadow of the whole of the large intestine below the splenic flexure disappears during defæcation (as in Fig. 11), showing that this part empties itself completely. In Fig. 10 the descending colon, iliac colon and part of the pelvic colon are still seen, as only a few small scybala were passed in spite of the active peristalsis which almost emptied the cæcum and ascending colon. This was no doubt due to the fact that the individual concerned put off defæcation for twelve hours after the desire was first felt, in order that we might be able to observe the act. Consequently water must have been absorbed from the fæces in the rectum, and the reflex brought about by voluntary contraction of the abdominal muscles and the diaphragm, at a time when the desire to defæcate was no longer felt, was insufficiently active to enable the rectum to rid

itself of the hard fæces it contained. The same explanation holds for the case shown in Fig. 12.

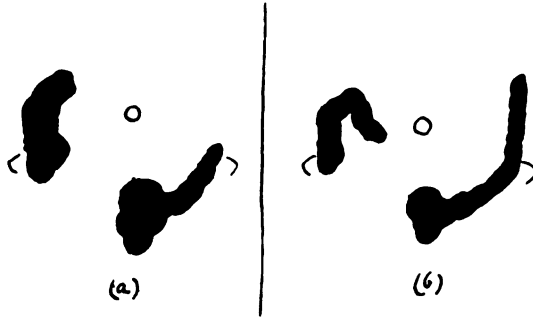
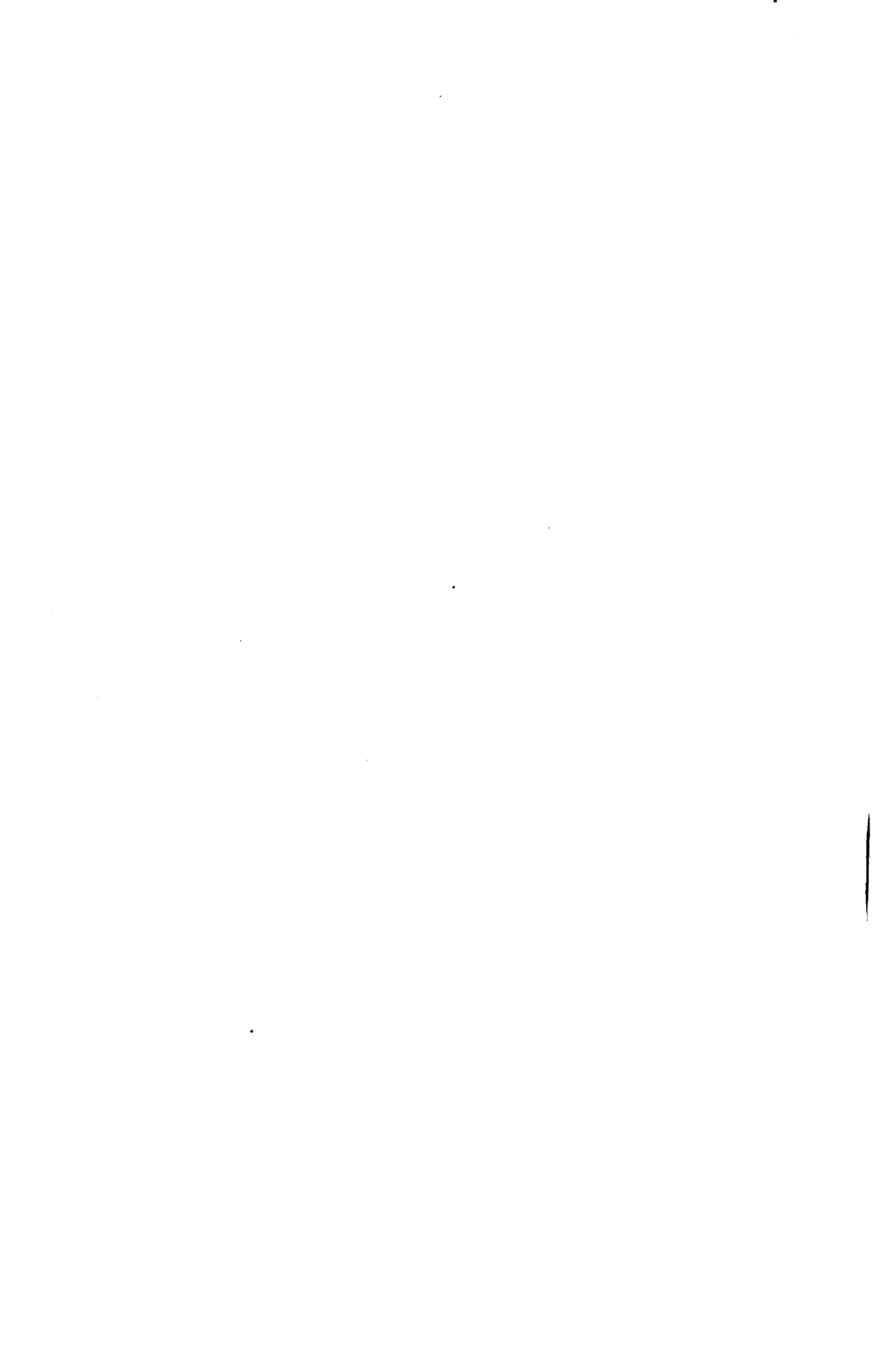


FIG. 12.—Normal defæcation. June 4th.—11 p.m., Bism. Carb., $\frac{3}{4}$ ss. June 5th.—9 a.m., violent desire to defæcate. Noon, Bism. Carb., $\frac{3}{4}$ ss. 8 p.m., tracing (a) made. Then defæcation, after which tracing (b) made.

If a bismuth breakfast be eaten one morning and the bowels are opened well the next morning, frequently some of the bismuth is found in the fæces. In a number of cases, however, it only appears in the fæces for the first time on the second morning after the bismuth breakfast. In one individual, whose stools passed at 8.30 a.m. were not abnormally soft or copious, all the bismuth taken on the previous morning was excreted, as no trace of a shadow could be seen when a skiagraphic examination was made at 10 a.m. Generally, however, the bismuth is not completely excreted for forty-eight hours, or sometimes for seventy-two hours. In one individual, who was not in the least constipated, but whose splenic flexure formed a very acute angle, a shadow was still present in the proximal part of the splenic flexure on three consecutive mornings following the day on which a bismuth breakfast had been taken. Already twenty-four hours after the meal the shadow was not very deep; the next morning it was fainter still, and on the third morning it could only be seen with difficulty.



THE SUBSEQUENT HISTORIES OF PATIENTS WHO HAVE RECOVERED AFTER OPERATION FOR PERFORATED GASTRIC OR DUODENAL ULCER.

By HERBERT FRENCH, M.A., M.D., F.R.C.P.

THERE has been considerable discussion lately upon the question whether or not a gastrojejunostomy should be performed at the same time that laparotomy and suture are undertaken for a perforated gastric or duodenal ulcer. Moynihan (*Med. Chir. Trans.*, London, 1907) is in favour of it, upon the ground that it minimises the chances of subsequent ill-effects from the ulcer. Paterson (*Hunterian Lectures, Lancet*, vol. i., 1906), is also in favour of it in some cases. There can, of course, be little doubt that the performance of gastrojejunostomy at the time of the operation for perforation is an additional tax upon the strength of the patient, if only on account of the extra minutes for which the anæsthesia and manipulation must be prolonged. The answer to the question whether such additional tax is advisable or not must depend in great part upon a comparison of the after-effects with and without the gastrojejunostomy respectively. If it were certain, for example, that without gastrojejunostomy the ulcer which has perforated is very liable to cause severe and chronic symptoms, pyloric stenosis, gastrectasis, subsequent perforations, severe hæmatemesis, or the like, and that gastrojejunostomy

rendered the patient much less likely to suffer from these after-effects, then there would be an argument of considerable weight in favour of gastrojejunostomy at the time of perforation; though even then it might be wiser to simply suture the perforation during the acute attack, leaving gastrojejunostomy to be performed after recovery from the peritonitis.

The crucial question is, therefore: Are the subsequent histories of patients who have recovered after simple suture of a perforated ulcer good or bad?

There are not a great many statistics upon the subject, but they are now beginning to accumulate. It is unfortunate that so many patients of the hospital class inevitably get lost sight of, otherwise the accumulation would be more rapid.

Mr. Crisp English (Med. Chir. Trans., 1903) found that only four out of fifteen cases had any gastric symptoms following the operation of closing the ulcer in St. George's Hospital. Mr. Paterson (*Lancet*, 1906) traced thirty-three cases, and found sixteen were perfectly well; fourteen had "dyspepsia," more or less severe, two requiring subsequent gastrojejunostomy, and one dying of a secondary perforation. Mr. Paterson's figures are certainly less favourable than those of Mr. Crisp English, but even so, half the patients that he traced were free from subsequent symptoms.

Guy's Hospital, up to 1905, discharged thirty patients recovered from perforated gastric or duodenal ulcer treated by laparotomy and suture; twelve of these have been lost sight of, but eighteen have been traced; these arrange themselves into two distinct groups, namely:—

- A. Those who have been free from gastric symptoms since their operation, and have been able to follow their laborious occupations as labourers, domestic servants, and so on: fifteen cases.
- B. Those who have suffered from dragging pains and other symptoms more or less severe, which render them quite unequal to their fellows in working power: three cases.

The following are notes about the individual patients:—

GROUP A.—Those who did well afterwards.

CASE 1.—William P., aged 43. He was admitted on July 30th, 1898, and was operated upon three hours after the perforation took place. The hole was upon the anterior surface of the stomach, near the cardiac end of the stomach. It was sutured, and the patient went out thirty-two days later. He had had lassitude, gastric pain after food, and nausea for two and a half years previously, but never hæmatemesis. He had seen many consultants. The condition had been repeatedly diagnosed as nervous dyspepsia, for which the patient had twice been sent for long voyages. In October, 1906, he came to show himself; he was strong and well, actively engaged in business, and he had had no gastric symptoms whatever since his operation. The scar was from the ensiform cartilage to the pubes, narrow and strong.

CASE 2.—Nellie R., aged 26. She was admitted on March 8th, 1900, and was operated upon seven hours after the perforation occurred. The hole was upon the anterior surface of the stomach, close to the pylorus: it was sutured; the abdomen was washed out and completely closed. The patient went out forty-three days later. Previous to the perforation she had had "indigestion" for two years on and off, with pains soon after eating, and occasional vomiting, but never hæmatemesis. In October, 1906, she writes, ". . . I am now married, and have been two and a half years out of London. I am most pleased to tell you that I have had splendid health, with no return of my old complaint whatever. Not only have I been free from pain, but I am quite able to eat anything in the way of fruit and vegetables, which I could never do before."

CASE 3.—M. He was operated upon for perforated gastric ulcer in 1900; the ulcer was simply sutured. The patient recovered well, and he had had no gastric symptoms since. In October, 1906, he was in good health, and busily engaged as a bank clerk.

CASE 4.—William S., aged 17. He was admitted on December 28th, 1901, and was operated upon four and a half hours after the perforation. The latter was in the duodenum. The ulcer was excised and the duodenum sutured. There had been no previous symptoms, the patient stating that he had not been ill in any way since he was a child. After the operation there was much local suppuration, and the wound took a long while to heal. There was still a sinus on discharge, ninety-one days after the operation. In October, 1906, he presented himself for examination. He had returned to his heavy work as a waterside labourer one month after he left the hospital, and had continued at it ever since without a bad symptom of any kind. When seen, he was a big strong healthy workman, with an abdominal scar ten inches long and two and a half inches wide in the middle line. The scar, though it looked thin and weak, showed no sign of developing into a ventral hernia, though the man wore no belt even at his heavy work.

CASE 5.—John R., aged 25. He was admitted on July 4th, 1903, and was operated upon five hours after the perforation. The latter was in the

anterior surface of the stomach, near the pylorus; it was simply sutured. The patient went out twenty-six days after the operation. Previously there had been epigastric pain after food for twelve months, with flatulence, but neither vomiting nor hæmatemesis. In October, 1906, he writes that he is actively engaged as a stevedore, and that he is perfectly well.

CASE 6.—Annie E., aged 21. She was admitted on March 12th, 1903, and was operated upon three hours after the perforation. The latter was upon the posterior surface of the stomach, near the pylorus. It was simply sutured, and the patient went out thirty-six days later. There had been no gastric symptoms previously, and no melæna. She writes in October, 1906, that: "I am very glad to be able to say that I am still continuing in the best of health." She works as a ward maid.

CASE 7.—Robert C., aged 43. He was admitted for perforated gastric ulcer upon September 4th, 1904. In October, 1906, he writes that: "While thanking you for your letter, I wish to say that I am very well. I have only had an occasional slight pain, which, perhaps, may not be due to the complaint." He works as a stoker.

CASE 8.—Isaac L., aged 35. He was admitted on March 30th, 1905, over twenty-four hours after perforation. At the operation two perforations were found, both in the stomach; one was a small hole in a big ulcer on the anterior surface, near the pylorus; the other was a small hole due to an acute ulcer on the anterior surface of the stomach near the cardiac end. Both were simply sutured. The patient went out thirty-five days afterwards. He was known to have had a gastric ulcer for a long time. He had had many severe attacks of hæmatemesis from 1897 onwards, but had always been able to work hard as a labourer between the attacks. In October, 1906, he writes that he is at work, and that "I am glad to say that I am getting on nicely and have had no pain since my operation."

CASE 9.—Beatrice L., aged 28. She was admitted on January 22nd, 1905, twenty-six hours after the perforation. The latter was in the stomach, near the pylorus, on the anterior surface towards the lesser curvature. There were many hindrances to her recovery. She developed pleurisy with broncho-pneumonia soon after the operation. The pleurisy led to effusion, and paracentesis thoracis was performed. After this she developed thrombosis of veins in her left arm and right leg, and an abscess in her right breast, which had to be opened and drained. Notwithstanding this, she went out 127 days after admission. In October, 1906, she writes: "I am pleased to be able to tell you I have been in the best of health since my discharge from the hospital." She works as a domestic servant. Previous to her admission she had suffered for three years from epigastric pains, which were worst half an hour after food, and she had had severe hæmatemesis twice.

CASE 10.—William G., aged 30. He was admitted on January 9th, 1905, fifty hours after the onset of symptoms of perforation. He had had "indigestion," but neither vomiting nor hæmatemesis, ever since his

return from the South African war eighteen months before. The perforated ulcer was on the anterior wall of the stomach, near, but not at, the pylorus. The hole was sutured and the patient left the hospital sixty-one days later. He writes in October, 1906: "My general health has been good since the operation; very occasionally I still have a little dyspepsia, which I suppose was the cause of my complaint, and which I put down to being compelled to lead an indoor life." He works as an indoor porter.

CASE 11.—William E., aged 26. He was admitted upon February 17th, 1905, and was operated upon six hours after the perforation. The latter was on the anterior surface of the stomach, near, but not at, the pylorus. It was simply sutured, and the patient left the hospital twenty-seven days later. Previously he had had neither vomiting nor hæmatemesis, but for three months had complained of "some discomfort" in the epigastrium about half an hour to one hour after meals. In October, 1906, he presented himself for examination. The scar, which was from the epigastric angle to the umbilicus, was strong and narrow. The man had been hard at work as a labourer since his discharge. He was looking as well as possible, and had no bad symptoms of any sort.

CASE 12.—Charles P., aged 48. He was admitted upon April 16th, 1904, for the usual symptoms, and was operated upon within a few hours of the onset of perforation. The hole was in the duodenum, one inch beyond the pylorus; it was simply sutured, and the patient went out thirty-nine days afterwards. Previously he had had "indigestion" badly for six years, with intervals of perfect health for four or five months at a time. There had been neither hæmatemesis nor melæna. In October, 1906, he writes: "I beg to state that my health is, and has been, very favourable indeed."

CASE 13.—William N., aged 48. He was admitted upon June 7th, 1899, and was operated upon within three hours of the onset of acute symptoms. The perforation was in the anterior wall of the stomach, near the pylorus. It was sutured. The patient went out fifty days later. He had suffered severely from "dyspepsia," which had started at a definite time seven years before; there had been epigastric pains which had become worse during the two and a half years preceding the perforation. There had been neither hæmatemesis nor melæna. He remained free from gastric symptoms for four years after the operation, and then he died of cerebral hæmorrhage.

CASE 14.—Caroline F., aged 22. This patient had twice suffered from, and survived, perforated gastric ulcer. The first time was in March, 1900; she was operated upon within twelve hours of the perforation, the ulcer being excised and the stomach sutured. She remained well until the end of 1904, when she had another sudden perforation, which was sutured. Since then she writes that she has remained in excellent health (October, 1906), working as a domestic servant. It is noteworthy that the second perforation occurred notwithstanding excision of the first ulcer. Previous to her first admission she had for two years had "indigestion pains" after food, with very occasional vomiting, but no hæmatemesis nor melæna.

CASE 15.—Robert B., aged 22. He was admitted on July 16th, 1904, and was operated upon within a very few hours of perforation. The hole was upon the anterior surface of the stomach, some way from the pylorus; it was sutured. The patient went out thirty-two days later. Previous to admission he had had gastric pains for two weeks only; he had hæmatemesis the day after the operation, but never before or since. In October, 1906, he came for examination. He was strong and well, and actively engaged as an engineer. His work took him to all parts of England and Scotland, and he had not been a day away from it since his recovery.

GROUP B.—*Patients who suffered from more or less severe after-effects.*

CASE 16.—Alice B., aged 36. She was admitted on October 28th, 1901, and was operated upon thirteen hours after the perforation occurred. The ulcer was upon the middle of the anterior surface of the stomach, half-way between the lesser and greater curvatures, and half-way between cardiac and pyloric orifices. The hole was sutured. The patient went out sixty-four days later. She remained well for a short time, but then began to suffer from severe dragging abdominal pains. In April, 1904, she was operated upon again; numerous adhesions were found; many of these were divided. The pains, however, persisted as before, and still do.

CASE 17.—Sophia G., aged 21. She was admitted in March, 1894, for the usual symptoms of perforated gastric ulcer. She had had no previous stomach symptoms. She was operated upon within a few hours of being taken ill. The ulcer was excised and the stomach sutured. She suffered from abdominal discomfort and pains in the abdomen during the next eighteen months, and in September, 1895, she was re-admitted, with typical symptoms of acute intestinal obstruction. An operation was performed; the obstruction was due to the kinking of a loop of small intestine which was adherent to the abdominal wall at the seat of the old scar. The patient died of pneumonia seven days afterwards.

CASE 18.—Frederick W., aged 34. He was admitted on February 6th, 1901, and was operated upon eight hours after the symptoms of perforation began. He had previously had "indigestion" for some months, but no vomiting, hæmatemesis, nor melæna. At the operation the ulcer which had perforated was found on the anterior surface of the stomach near the cardiac end. It was found impossible to suture the hole. The stomach was plicated so as to form a trough or channel for drainage from the perforation to the abdominal wound. A local abscess developed, and a sinus persisted for a long time. It was obvious at the time that many adhesions must result, and much deformity of the stomach. The man, a big, burly market-porter, has been almost incapacitated for work since. He has repeated recurrences of agonising abdominal pains. An operation for division of some of the adhesions was performed in November, 1901, and a gastrojejunostomy a little later. No relief followed even the latter. The pains are apparently due to dragging upon extensive adhesions, and not to the persistence of an ulcer, nor to any pyloric stenosis or dilatation of the stomach.

It seems needless to give the incomplete notes of the twelve cases that have not been subsequently traced. They have changed their addresses, and cannot be found. It is possible, of course, that they all did badly, though there is no evidence of this one way or the other. The present discussion must necessarily be confined to the cases that have been traced.

The following is a tabular summary of the eighteen cases:—

Sex. Age.					
1.	M. 43.	Perforated gastric ulcer.	Suture ...	Quite well	8½ years after.
2.	F. 26.	" gastric "	Suture ...	" 6½	"
3.	M. —	" gastric "	Suture ...	" 6	"
4.	M. 17.	" duodenal "	Excision and suture	" 4½	"
5.	M. 25.	" gastric "	Suture ...	" 3½	"
6.	F. 21.	" gastric "	Suture ...	" 3½	"
7.	M. 43.	" gastric "	Suture ...	" 2	"
8.	M. 35.	Two simultaneous perforated gastric ulcers.	Suture ...	" 1½	"
9.	F. 28.	Perforated gastric ulcer. Complications.	Suture ...	" 1½	"
10.	M. 30.	Perforated gastric ulcer.	Suture ...	" 1½	"
11.	M. 26.	" gastric "	Suture ...	" 1½	"
12.	M. 48.	" duodenal "	Suture ...	" 1½	"
13.	M. 48.	Perforated gastric ulcer. (Ultimately died of apoplexy.)	Suture ...	" 2½	"
14.	F. 22.	Perforated gastric ulcer. Second time.	Excision and suture	" 1½	"
15.	M. 22.	Perforated gastric "	Suture ...	" 2½	"
16.	F. 36.	" gastric "	Suture ...	Bad adhesions. Operation for division of these. Has bad pains.	
17.	F. 21.	" gastric "	Excision and suture	Intestinal obstruction by kinking of bowel 18 months after. Death.	
18.	M. 34.	" gastric "	Drained without suture.	Bad pains; not relieved by division of adhesions nor by gastrojejunostomy.	

One of the patients, it will be noticed, had had perforated gastric ulcer upon two separate occasions; most collections of statistics contain one or two examples of this, but upon the whole the liability to a second perforated gastric ulcer is not great. The case above was not one of those in which the

original ulcer persisted and perforated a second time, for the original ulcer was excised; it was a new ulcer, which formed and perforated some time after. It has been maintained that this is less likely to occur when gastrojejunostomy has been performed; even if this be the case, however, the liability to a second perforation is not great enough to afford any strong argument in favour of gastrojejunostomy at the time of laparotomy and suture.

It will be seen that of the eighteen cases of perforated gastric or duodenal ulcer which recovered after operation, and which have been subsequently followed up for periods varying from under two years to over eight years, fifteen, or 83 per cent., have done extremely well; whilst only three, or 17 per cent., have done badly.

These figures are, of course, for a comparatively small number of cases; but they are consecutive, and not selected. They agree very closely with the St. George's Hospital statistics compiled by Mr. Crisp English (*loc. cit.*).

Gastrojejunostomy was not performed in any of the cases at the time of suture. It is clear, of course, that if the ulcer which perforates has already led to pyloric stenosis, gastrojejunostomy is indicated either at the time or soon afterwards; but in the majority of cases which do badly the subsequent troubles are not due so much to the ulcer itself as to the perigastric adhesions resulting from the general peritonitis. Gastrojejunostomy would not be likely to minimise the formation of these adhesions to any great extent. The fact that so many of the patients do so well with simple suture is a considerable argument against the performance of the additional operation of gastrojejunostomy as a routine procedure at the time of laparotomy for the perforation of a gastric ulcer.

THE IMMEDIATE AND LATER RESULTS OF GASTROJEJUNOSTOMY FOR NON-MALIGNANT LESIONS OF THE STOMACH OR DUODENUM.

By R. P. ROWLANDS, M.S.,

AND

HERBERT FRENCH, M.D.

INTRODUCTION.

THE cases recorded in this paper embody all those that could be found in the Guy's Hospital Ward Reports up to the year 1905. They were collected together, and as many of the patients as possible were traced, with the object of ascertaining the late results of the operation, as a contribution by one of us to a special discussion on the subject at the Royal Medical and Chirurgical Society, in November, 1906.

The results are mainly of historical interest, and should not be taken too seriously as a measure of either the immediate or late results of gastrojejunostomy at the present time. Even in the last two years great improvements have been made in the technique of the operation; moreover, the general and local conditions of the patient are not allowed nowadays to deteriorate to a very low ebb before surgical treatment is adopted.

It must not be thought that the past results at Guy's Hospital have been either better or worse than those at other large hospitals which are situated in the midst of the London poor; the statistics brought forward at the above discussion proved this.

There can be little doubt that the greater the experience of the operator in gastric surgery, and the better the status of his patients, the more favourable will be his results. For these reasons, statistics based upon the work of picked surgeons are of less general utility than are those derived from a large hospital, in which the operations are performed by many different surgeons upon consecutive cases in whom the operation is only decided upon after consultation and great deliberation. The truth probably lies between the rosy picture drawn by a few surgeons of special experience and the more gloomy one below. When the Guy's Hospital statistics for the decade 1906-1915 are collected they will be much more favourable than those given here; but in the history of gastrojejunostomy the earlier results must necessarily be of value. It has been by studying the causes of failure in some of the earlier cases that physicians have recognised the wisdom of operating comparatively early in suitable cases, and surgeons have devised great improvements in the technique of the operation. (*Vide* p. 203.)

The following record must be regarded, therefore, as only applying to the results obtained in hospital practice previous to 1905; it will at least serve as a basis of comparison with a similar and much more favourable record that may be published in ten years time.

THE CASES.

The following are notes of the forty-seven cases that can be found in the Hospital Ward Reports up to 1905, arranged in groups according to the result:—

A. *Cases of Gastrojejunostomy for Non-malignant Conditions of the Stomach, in which death resulted within a fortnight of the operation.*

CASE 1.—Male, aged 28, admitted in April, 1895. The history was indefinite, except that there had been no hæmatemesis, and that for seven weeks there had been repeated vomiting of large quantities of fluid food.

The man was very thin. A lump was felt at the pylorus. This was thought to be carcinoma, so laparotomy was performed, and a posterior gastrojejunostomy by direct suture done. The patient died six days later of exhaustion. At the autopsy there was no peritonitis; the lump was not carcinoma, but a chronic simple ulcer with much matting, and partial stenosis of the pylorus.

CASE 2.—Male, aged 46, admitted in April, 1897. Two months previously he had swallowed two ounces of spirits of salts; he recovered from this, but soon after symptoms of pyloric obstruction set in. He was repeatedly sick every day. Anterior gastrojejunostomy was performed, a Murphy's button being used; vomiting was worse after the operation than it was before, and the patient died exhausted on the fifth day.

CASE 3.—Male, aged 52, admitted in January, 1898. There had been no trouble till twelve months previously, when persistent vomiting and signs of pyloric obstruction with dilated stomach set in. There was never hæmatemesis nor melenæ. At the operation fibrous stenosis of the pylorus was found; posterior gastrojejunostomy, with Halsted's method of suture, was performed. The patient did not gain strength after this, but sank and died on the thirteenth day. At the autopsy all the organs seemed healthy; there was no obvious dilatation of the stomach, no peritonitis, and no real obstruction to the pylorus.

CASE 4.—Male, aged 42, admitted in September, 1899. He had a fibrous cicatrix of the pylorus. Posterior gastrojejunostomy was performed, a Murphy's button being used. The patient died of shock within twenty-four hours.

CASE 5.—Female, aged 51, admitted in September, 1900. She was found to have a cicatrising ulcer of the pylorus. Gastrojejunostomy was performed, a Murphy's button being used. The patient died on the sixth day of general peritonitis. At the autopsy it was found that no union between stomach and jejunum had taken place; the button was free within the stomach.

CASE 6.—Male, aged 43, admitted in November, 1900. He was found to have a cicatrising pyloric ulcer. Anterior gastrojejunostomy by direct suture was performed. The patient died on the ninth day of syncope. At the autopsy it was found that the jejunum had become doubled round a peritoneal band.

CASE 7.—Male, aged 67, admitted in January, 1902. He was found to have a cicatrising and leaking pyloric ulcer. Anterior gastrojejunostomy was performed, a Murphy's button being used. There was continual vomiting after the operation, and pneumonia supervened. The patient died on the thirteenth day. At the autopsy the button was found in the duodenum.

CASE 8.—Male, aged 46, admitted in June, 1902. He was found to be suffering from peri-pyloritis. Anterior gastrojejunostomy by direct suture was performed. The patient developed broncho-pneumonia, and died on the fifth day.

CASE 9.—Male, aged 42, admitted in February, 1903. He was found to have a cicatrised pyloric ulcer. Posterior gastrojejunostomy by suture was performed. Vomiting after the operation was so extreme that a second operation was performed next day, and jejunostomy done. The patient died the day after. At the autopsy there was no peritonitis, and no obvious obstruction to the bowel.

CASE 10.—Female, aged 25, was admitted in March, 1904, for dilated stomach, and apparent pyloric obstruction. At the operation the trouble was found to be due to a cicatrising duodenal ulcer. Posterior gastrojejunostomy by means of a Murphy's button was performed. Symptoms of acute peritonitis set in on the second day, and the patient died on the third day after the operation. At the autopsy the gastrojejunostomy was found to be all right, but the duodenal ulcer had itself perforated and caused the peritonitis.

CASE 11.—Male, aged 47, was admitted in January, 1905, for traumatic cicatrix of the pylorus. Antero gastrojejunostomy was performed by means of a Murphy's button, and entero-enterostomy was done at the same time. The patient died of shock and collapse on the third day.

CASE 12.—Female, aged 44, was admitted in November, 1902, for excessive and repeated hæmatemesis. Anterior gastrojejunostomy was performed by means of a Murphy's button. The hæmatemesis persisted after the operation as badly as before; a second operation was performed, gastrotomy done, and search made for the bleeding point. The patient died on the sixth day exhausted and blanched from further hæmorrhage. At the autopsy the intestines were full of blood; the stomach contained no ulcer, nor could any erosions or other abnormality be seen.

CASE 13.—Male, aged 18, was admitted in January, 1905, for repeated hæmatemesis and blanching. Anterior gastrojejunostomy by means of a Murphy's button was performed. When the stomach was opened general oozing from the gastric mucosa was seen, but no ulcer. The patient died on the second day collapsed from further hæmorrhage. At the autopsy the intestines were full of blood; there was no ulcer; on careful searching multiple minute hæmorrhagic erosions were found in the gastric mucosa.

B. Cases of Gastrojejunostomy for Non-malignant Conditions of the Stomach in which Recovery from the Operation occurred, but in which no Relief to the Symptoms Resulted.

CASE 14.—Male, aged 53, was admitted in October, 1895. He had been quite well till February, 1891, when he first had severe epigastric pain lasting on and off for four months. At that time he had neither hæmatemesis, melæna, nor vomiting. In December, 1894, the pains recurred; a week later he brought up three pints of vomit containing altered blood. Since then he had had copious vomiting at intervals; as much as sixty-eight ounces were measured at a time. On November 12th, 1895, posterior gastro-

jejunostomy by means of a Murphy's button was performed. The diagnosis of cicatrised pyloric ulcer was confirmed. He passed the button *per rectum* on December 6th. The vomiting persisted after the operation, occurring on November 13th, December 2nd, 6th, 12th, 18th, and 23rd, in hospital, and at similar intervals since discharge.

CASE 15.—Male, aged 36, was admitted in March, 1902, for symptoms which suggested perigastric adhesions. He had previously been successfully operated upon for perforated gastric ulcer. Posterior gastrojejunostomy was performed. It is not stated whether a Murphy's button was used or not. No relief to his symptoms followed the operation.

CASE 16.—Female, aged 40, was admitted in August, 1903, for the usual symptoms of pyloric obstruction. Gastrojejunostomy was performed by means of a Murphy's button. It is not stated whether the gastrojejunostomy was anterior or posterior. The diagnosis of cicatrising ulcer of the pylorus was confirmed at the operation. There was no relief to the symptoms even at the time, and the patient died of exhaustion six months later.

CASE 17.—Female, aged 45, was admitted in March, 1905, for the usual symptoms of pyloric obstruction. The diagnosis of cicatrising gastric ulcer was confirmed at the operation. Posterior gastrojejunostomy by means of a Murphy's button was performed. The symptoms persisted after the operation as badly as before.

CASE 18.—Female, aged 40, was admitted in March, 1905, for the usual symptoms of pyloric obstruction. The diagnosis of cicatrising gastric ulcer was confirmed at the operation. There were extensive perigastric adhesions, and great dilatation of the stomach. Posterior gastrojejunostomy by means of a Murphy's button was performed. On discharge the dilatation of the stomach was no less than before the operation, and the symptoms persisted as before.

CASE 19.—Female, aged 42, was admitted in June, 1902, for the usual symptoms of pyloric obstruction. At the operation the diagnosis of cicatrising gastric ulcer was confirmed. The stomach was moderately dilated. Posterior gastrojejunostomy by means of a Murphy's button was performed. There was no relief to the symptoms after the operation, and the patient died five months later of exhaustion. At the autopsy the cicatrised ulcer was found to have nearly, but not quite, occluded the pylorus; *the gastrojejunostomy opening had become completely closed by cicatrisation*, and the Murphy's button was free inside the stomach.

C. *Cases of Gastrojejunostomy for Non-Malignant Conditions of the Stomach in which Recovery from the Operation occurred, with Relief for a short time, but subsequent Recurrence of the former symptoms.*

CASE 20.—Male, aged 47, was admitted in March, 1900, with all the symptoms of dilated stomach from pyloric obstruction. The trouble began

eighteen months previously, when he first suffered from acute epigastric pains, which were worst one hour after meals, but lasted as much as six or eight hours after the last meal of the day, so that he was kept awake at night. Later he vomited copiously two or three times a week. He had had no hæmatemesis, and had noticed no melæna. At the operation a chronic duodenal ulcer was found, and a much dilated stomach. Anterior gastrojejunostomy by means of a Murphy's button was performed. There was great relief for a short time, but, within a month of his discharge, the symptoms were all back again. He was re-admitted in September, 1900, but declined further operative measures, and was discharged two days later *in statu quo antea*.

CASE 21.—Male, aged 43, was admitted in March, 1903. Fifteen years previously he began to suffer from acute epigastric pains after food, relieved by vomiting. He had had neither hæmatemesis nor melæna. For one and a half years he was quite unable to work; he attended as an out-patient, and ultimately, by careful dieting and medicinal treatment, became quite well, and for thirteen years had no return of the symptoms, and was able to work hard. In 1902 vomiting and pain recurred; a gastrojejunostomy was performed, and the diagnosis of pyloric cicatrix confirmed. Slight relief followed, but then the symptoms all recurred, and grew worse and worse. When seen in 1903, five months after the operation, he could not stand up straight on account of the pains in his abdomen, and there was a large ventral hernia of the scar, which bulged extremely on coughing. It was decided that nothing more could be done.

CASE 22.—Female aged 36, was admitted in February, 1904, for the symptoms of cicatrising ulcer of the pylorus. The diagnosis was confirmed at operation. Gastrojejunostomy by means of a Murphy's button was performed. On discharge she seemed relieved, but shortly afterwards the old symptoms returned, and she has been re-admitted several times since for lavage of the stomach, which temporarily relieves her.

CASE 23.—Female, aged 26, was admitted in February, 1905, for perigastric adhesions after a perforated gastric ulcer. It was also thought that there was some pyloric obstruction. Posterior gastrojejunostomy was performed by means of a Murphy's button. She experienced great relief at the time, but three months later all her symptoms had returned as badly as before.

CASE 24.—Female, aged 33, was admitted in January, 1904, having never passed a week since April, 1900, without vomiting. After food she had severe pain at the umbilicus. The vomit occasionally contained blood. She was operated upon; an old fibrosed gastric ulcer was found, the pylorus not being stenosed. Posterior gastrojejunostomy by Murphy's button was performed. The patient vomited incessantly for eleven days after the operation, and nearly died. The button was passed *per rectum* on the twenty-fourth day. On discharge she still had severe pains in the abdomen; she was kept awake at night by them, and she was sick as before.

D. Cases of Gastrojejunostomy for Non-malignant Conditions of the Stomach, in which great relief resulted, and in which either cure or great improvement is maintained.

CASE 25.—Male, aged 30, was admitted in December, 1901. At the operation peritoneal adhesions around the pylorus were found. Posterior gastrojejunostomy was performed with the aid of a Murphy's button. Relief to the previous symptoms was complete, and the patient reported himself "cured" four and three quarter years later.

CASE 26.—Male, aged 39, was admitted in January, 1902, for symptoms of pyloric obstruction. At the operation a cicatrised ulcer of the pylorus was found. Posterior gastrojejunostomy was performed by suture. The patient remained "cured" for three and a quarter years, and then died of acute phthisis.

CASE 27.—Female, aged 23, was admitted in December, 1902, for symptoms of gastric ulcer. The trouble began in 1898 with epigastric pains after food, beginning immediately after a meal, and lasting two hours. A little later vomiting occurred repeatedly, the amount of vomit being the food just taken. The symptoms came and went. Hæmatemesis occurred once in 1899 and twice in 1902, the attack being very severe, one month before admission. She was vomiting everything she took, so posterior gastrojejunostomy by suture was performed. At the operation the diagnosis of pyloric cicatrix from simple ulcer was confirmed. There were many peritoneal adhesions around the pylorus, but the stomach was not dilated. On discharge, one month after the operation, she was able to take full diet without the least discomfort, and two and a half years later she reports herself "cured."

CASE 28.—Male, aged 46, admitted in May, 1904, for pyloric obstruction and dilated stomach. The trouble dated from seventeen years previously, since when he had always been liable to acute "indigestion" pains, and occasional vomiting. He had never had hæmatemesis nor melæna. Latterly the pains had been acute and almost continuous even upon milk diet, and he had begun to vomit great quantities of fluid at intervals. He was wasted, thin, and anæmic. At the operation many adhesions were found around the pylorus; the condition of the ulcer is not stated. Posterior gastrojejunostomy was performed by the aid of a Murphy's button, which was passed on the fourteenth day. On discharge he was still very weak, and had some pains even on careful diet, but he was much better. One and a quarter years later he reports himself as "improved, but not free from pains after food."

CASE 29.—Male, aged 65, was admitted in July, 1904. At the operation a cicatrised pyloric ulcer was found. Anterior gastrojejunostomy was performed with the aid of a Murphy's button. Relief to his symptoms was immediate, and one year later he reports himself as "cured."

CASE 30.—Male, aged 64, was admitted in November, 1904, for symptoms of pyloric obstruction. At the operation a chronic ulcer was found; it is not stated whether it was in the duodenum or at the pylorus. The stomach was

moderately dilated. The symptoms dated from only two years previously, and consisted mainly in acute pains "in the chest" coming on from two to three hours after food. Vomiting had been slight; neither hæmatemesis nor melaena had occurred. Gastrojejunostomy was performed by direct suture, and jejunio-jejunostomy was done at the same time. Relief was immediate, and nine months later he reports himself "much improved."

CASE 31.—Male, aged 40, was admitted in January, 1905, for chronic duodenal ulcer. The diagnosis was confirmed at operation. Posterior gastrojejunostomy was performed with the aid of a Murphy's button. Relief was immediate, and one year later he reports himself "cured."

CASE 32.—Male, aged 32, was admitted in June, 1905. He had recovered from a perforated duodenal ulcer two months before, and was now admitted for pains which were thought to be due, in part at least, to adhesions. Gastrojejunostomy was performed, and he reports six months later that he has remained quite free from the pains.

E. The following cases complete the list of all the Gastro-jejunostomies that have been performed in Guy's Hospital up to 1905 for Non-Malignant Conditions; but none of them have been traceable since discharge from the Hospital.

CASE 33.—Male, aged 34, was admitted in October, 1900. At the operation a cicatrised pyloric ulcer was found, with many surrounding adhesions. Gastrojejunostomy, with the aid of a Murphy's button, was followed by great relief up to the time of his discharge.

CASE 34.—Male, aged 39, had for nine years suffered from very bad epigastric pains at intervals of three or four months. He had had but slight vomiting and no hæmatemesis. Medicinal treatment and dieting had always given relief until three years ago, since when the pains had been frequent and very acute. In 1898 he was operated upon for gallstones, but none were found. In July, 1899, he was admitted with a view to further operation. He improved so much with rest in bed, that laparotomy was postponed. Immediately on going out the pains returned. In October, 1899, he was readmitted. Partial stenosis of the pylorus from perigastric adhesions was found on operating; the pylorus was digitally dilated, after opening the stomach. Relief followed, but it was temporary only. Pains began to recur six weeks later. In June, 1900, the pains were so bad that gastrojejunostomy was performed. Relief followed at once, but the patient has been lost sight of since.

CASE 35.—Male, aged 50, was admitted in May, 1901, for the usual signs of pyloric obstruction. At the operation, a cicatrised pyloric ulcer was found. Posterior gastrojejunostomy was performed by means of a Murphy's button. The patient recovered, with considerable relief, but has been lost sight of.

CASE 36.—Male, aged 37, was admitted in May, 1901, for simple pyloric obstruction. Pyloroplasty had been performed fourteen months previously, after he had suffered from repeated abdominal pains and vomiting on and off for ten years. The symptoms rapidly recurred after the pyloroplasty, so posterior gastrojejunostomy was performed with the aid of a Murphy's button. The patient was "cured" on discharge, but has not been traced since.

CASE 37.—Male, aged 50, was admitted in December, 1901, for pyloric stenosis. At the operation posterior gastrojejunostomy was performed with the aid of a Murphy's button. The symptoms were "much improved" on discharge.

CASE 38.—Male, aged 39, was admitted in April, 1902, for pyloric stenosis, the result of swallowing corrosive acid. Gastrojejunostomy was performed with the aid of a Murphy's button. The patient was "cured" on discharge.

CASE 39.—Male, aged 36, was admitted in September, 1902, for cicatricial stenosis of the pylorus. Posterior gastrojejunostomy was done with a Murphy's button. He was apparently cured on discharge.

CASE 40.—Male, aged 32, was admitted in December, 1902, for persistent vomiting. The cause was not found. At the operation it was noted that there was no pyloric stenosis, and no ulcer either in the stomach or in the duodenum. The stomach was moderately dilated. Posterior gastrojejunostomy with a Murphy's button was performed. Very severe vomiting persisted for four days afterwards, but then ceased, and the patient on discharge was apparently cured.

CASE 41.—Female, aged 30, was admitted in March, 1903. Two years previously she had been successfully operated upon for perforated gastric ulcer. Since then she had had three bouts of acute epigastric pain, and it was for one of these that she was now re-admitted. The ulcer, which had previously perforated, had been on the anterior surface of the stomach near the cardiac end. There was no pyloric obstruction, and the pains seemed due to the many perigastric adhesions rather than to the ulcer. Posterior gastrojejunostomy by suture was performed; the patient was discharged free from pains.

CASE 42.—Female, aged 37, was admitted in November, 1903. She began to suffer from great pain in the front of the chest and from vomiting twelve months previously. During all that time she had vomited almost continuously, retaining even milk with the greatest difficulty. On one occasion only was there hæmatemesis, one pint. At the operation an ulcer was found on the lesser curvature of the stomach, the base being adherent to the liver. The pylorus was free, and there was no gastrectasis. There were many recent perigastric adhesions. Posterior gastrojejunostomy by suture was performed. On discharge the patient retained simple foods, but required to be most careful with her diet. She has not been traced.

446 *The Immediate and Later Results of Gastrojejunostomy*

CASE 43.—Male, aged 59, was admitted in May, 1902, for cicatrising pyloric ulcer, verified by operation. Posterior gastrojejunostomy was performed; the patient was discharged greatly relieved.

CASE 44.—Female, aged 49, was admitted in January, 1902, for pyloric obstruction, which was found, at operation, to be due to a calcified retro-peritoneal cyst. Posterior gastrojejunostomy with Murphy's button was performed. Improvement was great, and the patient was well on discharge.

CASE 45.—Female, aged 50, was admitted in January, 1905, for symptoms of pyloric obstruction. Operation showed the condition to be a chronic duodenal ulcer. Posterior gastrojejunostomy, with a Murphy's button, was performed, and on discharge the patient was well.

CASE 46.—Male, aged 38, was admitted in February, 1905, for pyloric stenosis. A cicatrised pyloric ulcer was found at operation. Anterior gastrojejunostomy by suture was performed, and the patient was quite well on discharge.

CASE 47.—Female, aged 27, was admitted in March, 1905, for abdominal pains after recovery from a perforated gastric ulcer. At the operation perigastric adhesions were found; posterior gastrojejunostomy, with a Murphy's button, was performed, and the patient was discharged better, but not quite free from pains.

THE NATURE OF THE OPERATIONS PERFORMED.

Murphy's button was used in thirty-one cases, direct suture in eleven, and in five the method of anastomosis is not stated. The anterior operation was adopted in ten cases, the posterior in twenty-seven, and in ten it is not known whether the opening was anterior or posterior. In two cases, Nos. 11 and 30, entero-anastomosis was performed at the same time.

If the whole number are arranged broadly into three groups, it will be found that:—

	Murphy's Button.	Direct Suture.	Not stated.	Anterior.	Posterior.	Not stated.
Of those who died within a fortnight	8	5	0	7	4	2
Of those who survived, but got no relief	5	0	1	0	5	1
Of those who survived, and got relief for a time at least	18	6	4	3	18	7

The total number of cases is so small that they do not afford any reliable basis for drawing conclusions as to the merits of direct suture as against Murphy's button. It must be remembered that during the years when the above operations were performed it was the custom to make the anastomotic opening very little, if any, larger when direct suture was employed, than the one formed by the Murphy button. It is only recently that the need for a large opening between the stomach and intestine has been fully realised, and the time has not yet come for comparing the results of these large openings by direct suture with those of Murphy's button. A discussion of this question will be found on page 191. As regards the relative merits, or at least the immediate safety or the reverse, of the anterior and posterior operations, the figures seem to argue strongly against the former. Seven out of the ten anterior gastrojejunostomies were fatal, whereas only four out of the twenty-seven patients submitted to posterior jejunostomy died.

A GENERAL SUMMARY OF THE CASES.

It is interesting to note that, whereas the older teaching in regard to gastric ulcer was that females were affected more than males, and that the commonest age for it was under thirty, the above cases include :—

31 males, and
16 females.

And the ages of the patients were as follows :—

Aged less than 20 years	1
Between 20—30	"	7
30—40	"	17
40—50	"	15
50—60	"	4
60—70	"	3

This is an argument in favour of the modern view that gastric ulcer used to be diagnosed in young women upon insufficient grounds, unless it be assumed that ulcers in them heal without the effects that are produced in men.

There were only two cases in which gastrojejunostomy was performed for severe hæmatemesis. The operation failed to arrest the bleeding, and death resulted; in both patients the stomach was actually observed during life to be oozing blood from many points and not from a single focus that could be dealt with by any surgical means. The cases were examples of gastrostaxis of which Dr. Hale White has collected a great many. It is exceedingly difficult to distinguish these cases clinically from those of hæmorrhage from actual gastric ulcer, and it is now the general opinion that surgical measures are contraindicated whilst gastric bleeding is going on. Hæmatemesis, if it recur with increasing severity at diminishing intervals, may demand operation, but the latter should be performed during a quiescent period and not during active hæmorrhage.

The condition calling for operation in the remaining forty-five cases was almost without exception a chronic cicatrising ulcer either of the stomach or of the duodenum, in most cases causing obstruction. Thus there were thirty-four with definite pyloric stenosis and six with duodenal ulcers; in only seven was there no actual obstruction, but in six of these there were extensive perigastric adhesions, due in three cases to a former acute perforation. Moreover, in the great majority the symptoms had existed for a long time. These are most important points in connection with the mortality. It is easy to understand that statistics which include any considerable proportion of cases in which gastrojejunostomy has been performed for simple ulcer without pyloric obstruction are likely to be much more favourable.

Eleven cases, or over 23 per cent., died within a fortnight of their laparotomy. The causes of death were as follows:

Simple exhaustion accounted for	...	3 cases.
Continued vomiting	2 "
Shock	2 "
Peritonitis from non-union	1 "
" perforation of the ulcer		1 "
Pneumonia	1 "
Kinking of the small intestine by a band		1 "

And death occurred :—

Within twenty-four hours in	2 cases.
On the 2nd day in	1 "
3rd "	2 "
5th "	2 "
6th "	2 "
9th "	1 "
13th "	2 "

This high mortality is much the same as that at other hospitals during the same period ; at St. Thomas's Hospital it was 23 per cent. for the same years, and at St. Bartholomew's it was 21 per cent. in nineteen gastrojejunostomies performed for pyloric stenosis between 1903 and 1905.* It must be borne in mind that the patients almost all had had their trouble for years, and that their general health was, therefore, much below par at the time of operation. The mortality for gastrojejunostomy performed in a series of perfectly healthy men would, no doubt, be extremely small. The above statistics overstate the direct risk of the operation, especially if cases be carefully selected ; but the risk of gastrojejunostomy for cicatrization of pyloric ulcers certainly cannot be called a small one.

Turning next to the remote results, it will be seen that even when the operation is in itself successful the subsequent condition of the patients is not by any means always good. Of the forty-seven consecutive cases collected there remain thirty-four, when those who died at once are deducted. Nineteen of these have been traced ; the remaining fifteen were discharged much relieved, and what happened to them afterwards is unknown. For the sake of argument, let it be assumed that they have since remained absolutely well. Six of the nineteen who recovered, and have been traced, got no relief to their symptoms, even for a time, one dying six months after ; five, though they obtained relief for a short time, had all their old symptoms back again within a few months. That is to say, the result is known to have been a failure in *thirty-two per cent.* of the cases who recovered from the

* Vide Roy, Med. and Chir. Soc. Trans., 1907.

450 *The Immediate and Later Results of Gastrojejunostomy
for Non-malignant Lesions of the Stomach or Duodenum.*

operation. The result is known to have remained good in eight only:—

In	1	for between	4—5	years.
	1	"	3—4	"
	1	"	2—3	"
	3	"	1—2	"
	2	"	1—1	"

The ultimate results in the remainder are not known, but the 32 per cent. of failures is based on the presumption that the untraced cases all did well.

The net result of these statistics is, therefore, that all the cases died in whom gastrojejunostomy was performed for hæmorrhage; that over 23 per cent. died as the result of the operation; and that at the very least 32 per cent. of the cases who recovered got no lasting relief from their operation.

Some of the reasons why the results of gastrojejunostomy in the last decade are not more satisfactory have already been indicated. The risks at the present time are probably much less than they have been in the past. Nevertheless, taking the cases all round, the performance of gastrojejunostomy, even at the present time, does carry with it a real risk to the patient's life; it is an operation which should not be decided upon with any sort of haste. When it is done for the purpose of making a new passage for the food onwards from the stomach when the proper path through the pylorus is interfered with by an ulcer, by a scar, or by adhesions, one must not give one's patient's friends too bright a picture of the results to be expected, or in many cases there is sure to be disappointment.

SPECIMENS RECENTLY ADDED TO THE PATHOLOGICAL MUSEUM.

BY LAURISTON E. SHAW, M.D.,

AND

JOHN FAWCETT, M.D.

INJURIES AND DISEASES OF THE ARTERIES.

2657 Abnormal Origin of Coronary Artery.

The base of a heart with the first part of an aorta laid open to show one of the coronary arteries arising from the aorta half an inch above the point of union of two of the semilunar valves. The other artery arises in the normal position.

Thomas K. L., æt. circa 55, was admitted under Dr. Goodhart in a comatose state, and died from cerebral hæmorrhage. *See Insp.*, 1889, No. 340.

2681 Aneurysm of the Innominate Artery opening the Trachea.

The base of a heart with the aorta and its main branches. Between the innominate and left carotid arteries is seen a globular aneurysmal sac about the size of a walnut. The orifice of the aneurysm is situated on the left wall of the innominate artery just below its point of division. The anterior wall of the sac has been removed and the blood-clot, which it contained, turned out to show the cartilages

laid bare. On the reverse of the specimen the small opening in the trachea is seen partially occluded by blood-clot. The aorta is extremely atheromatous and the arch dilated.

James R., æt. 42, was admitted under Dr. Taylor for cough and dyspnoea. The cough was high-pitched and brassy, and tracheal tugging was present. Three days later a gradually increasing pulsation was noticed above the manubrium. Five days after admission the patient had a severe fit of coughing, brought up a pint of bright frothy blood, and died almost immediately. At the autopsy a quantity of blood was found in the bronchial tubes, some in the oesophagus, and a large moulded clot in the stomach. *See Insp.* 1899, No. 71.

2684 Ruptured Aneurysm of the Internal Carotid Artery.

The arteries of the base of a brain dissected to show an aneurysm, seven-eighths of an inch long and half an inch in diameter, springing from the left internal carotid artery just before its bifurcation. There is a large rent in the wall of the sac from which the fatal hæmorrhage occurred.

Mary C., æt. 34, was admitted on December 29th, 1893, under Dr. Hale White. She had always been subject to severe headaches. On December 25th, while at dinner, she suddenly fell off her chair, and when picked up was unconscious. On recovery from this attack she was very sick, and complained of intense headache. On January 2nd, 1894, partial right facial paralysis was present, followed later by ptosis of the left eye. On January 7th there was complete paralysis of the left third nerve. The severe headache persisted, and patient developed great pain down the spine. On January 16th patient became delirious and semiconscious, with twitchings of the face and arms. She died three weeks after admission, having become quite unconscious. At the autopsy a large amount of blood-clot was found in the subdural and subarachnoid spaces. The clot had extended into the fourth ventricle and also into the subarachnoid space around the spinal cord, where it formed a layer an eighth of an inch thick. With the exception of the affected vessel, the cerebral arteries were healthy. The heart was normal, and there was no evidence of syphilis. *See Insp.* 1894, No. 33, and *Trans. Clinical Soc.*, vol. 28, 1895.

2685 Ruptured Aneurysm of the Internal Carotid Artery.

The central portion of the base of a skull mounted to show, projecting from the position of the right cavernous sinus, the ovoid sac of an aneurysm measuring about three-quarters of an inch in its antero-posterior diameter. The

aneurysm, which is filled with blood-clot, springs from the internal carotid artery just at its termination.

John W., *æt.* 21, was admitted under Dr. Hale White in a state of coma, having suddenly become unconscious and fallen down while carrying a sack of coal. He had been complaining of pain of a neuralgic character in the right temporal region for some weeks. With the ophthalmoscope, a well-outlined area of red-brick tint was seen in both eyes, encroaching on the disc on the right side. At the autopsy a considerable amount of blood-clot was diffused over the pia mater, and especially over the front and inner side of the temporo-sphenoidal lobe. The retina was separated from the choroid by blood. There was no evidence of syphilis, and the cerebral arteries, with the exception of the affected vessel, were healthy. See *Insp.* 1894, No. 40, and *Trans. Clinical Soc.*, vol. 28, 1895.

2699 Aneurysm of the Radial Artery.

A portion of a radial artery removed during life, together with a spherical aneurysmal sac which springs from it and measures half an inch in its longest diameter. It is filled with firm blood-clot.

Agnes Gertrude H., *æt.* 15, was admitted under Mr. Howse with an aneurysm of the right radial artery. She had cut her wrist five weeks previously, severing the radial artery. A week after, when the splint upon which the arm had been fixed was removed, a pulsating swelling was detected. The operation wound healed by first intention, and the patient left the hospital twelve days after the operation had been performed. See *Surgical Reports, Mr. Howse*, 1902, No. 112.

2705 Ruptured Aneurysm of Mesenteric Artery.

A portion of the transverse meso-colon from which the superjacent colon has been turned upwards to show the partially dissected vessels. The vessels are nearly all filled with blood-clot, and in the lowest branch there are two small aneurysmal dilatations, both containing thrombus, the larger presenting a small opening through which fatal hæmorrhage took place.

Frederick H., *æt.* 45, was admitted under Dr. Pitt with general weakness, anæmia, and œdema of the legs. Albumen, blood, and epithelial casts were present in the urine. The patient became rapidly weaker and died nine days after admission. At the autopsy twenty-five ounces of fluid blood and thirteen ounces of blood-clot were found in the peritoneal cavity. The kidneys presented a "flea-bitten" appearance on the surface, and on section the aspect of an acute tubal nephritis. See *Insp.* 1904, No. 361.

2717 Cured Popliteal Aneurysms.

Two aneurysmal sacs completely filled with ante-mortem thrombus. They were removed after death, together with portions of the femoral artery. The vessels above the aneurysms are occluded by blood-clot.

William U., æt. 54, was admitted under Dr. Taylor with signs of aortic incompetence and an enlarged heart. The patient had been previously under the care of Mr. Davies Colley with an aneurysm in each popliteal space, for the relief of which the femoral arteries were successfully ligatured. At the autopsy the aorta was found to be extremely atheromatous throughout, with a fusiform dilatation of its first part involving the arch. *See Insp.* 1891, No. 431.

2719 Varicose Aneurysm of the Common Iliac Vessels.

An inferior vena cava with the abdominal aorta and their main divisions seen from behind. The posterior walls of the veins have been removed to show the left common iliac greatly distended and presenting at its upper part a smooth rounded opening through its anterior wall, whereby an indirect communication is established with the aorta. On the reverse of the specimen the aorta has been laid open to show, at its bifurcation, an opening leading into an aneurysmal sac situated immediately behind the right common iliac artery. The sac, which is somewhat flattened from before backwards, has thick fibrous walls, and measures about an inch and a half in diameter.

William N., æt. 5, was admitted under Dr. Pitt for œdema of the left leg and mitral regurgitation. This was gradually followed by ascites, pleural effusion, and œdema of the right leg, and the boy died two months later of cardiac failure. Three months before admission the patient had been struck in the left groin by a truck. At the autopsy the heart was found to be dilated and hypertrophied; there was thrombosis of some of the branches of the left iliac vein, and the veins of the left side of the penis were varicose. *See Insp.* 1892, No. 384.

2721 Calcareous Embolus in Cerebral Artery.

Vessels dissected from the base of a brain to show in the right middle cerebral artery a small calcareous embolus, which in the recent state was found to have occluded the lumen of the vessel.

Thomas M., *æt.* 42, was admitted in October, 1893, under Dr. Pye-Smith, with aortic incompetence and left hemiplegia of a few days' duration. The use of the limbs gradually improved and he went home, but died a few days later. At the autopsy the area of the brain corresponding to that supplied by the thrombosed vessel was found to be undergoing softening. The left ventricle was considerably enlarged, the aortic cusps were shrunken and incompetent, with large calcareous masses of vegetations attached to them. *See Insp.* 1893, No. 36.

2725 Thrombosis of the Innominate Artery.

A portion of the arch of an aorta much affected by atheroma. The orifice of the innominate artery is seen to be completely occluded by thrombus, which extends into and partially fills the main branches of the vessel.

Albert A., *æt.* 44, was admitted under Dr. Hale White for cough, dyspnoea, and oedema of the legs. The symptoms first appeared fourteen days previously. He was found to have signs of aortic incompetence, and no pulse could be detected in the arteries of the neck or upper extremity on the right side. Three days later he had a convulsive attack, followed by inability to articulate, ptosis, and complete ophthalmoplegia on the left side, with paralysis of the internal rectus on the right side. The following day facial paralysis appeared, and later the right arm and leg were paralysed and the pupils minutely contracted. At the autopsy the cerebral vessels were found to be thickened and atheromatous, and there was an embolus in the basilar artery. The heart was dilated and hypertrophied, and the aortic valves shrunken and thickened. The aorta was somewhat dilated in its first part and very atheromatous throughout. There was a recent infarct in one lung and evidence of old infarctions in the spleen. *See Insp.* 1898, No. 424.

2729 Thrombosis of the Basilar Artery.

A portion of the base of a brain with the basilar artery laid open to show its distal portion occupied by a firm thrombus, which extends into some of the smaller vessels.

Alfred A., *æt.* 44, was admitted under Dr. Hale White with oedema of the legs of fourteen days' duration, and evidence of aortic incompetence. No pulse could be felt in the arteries of the upper extremity nor in the right carotid artery. Three days later he had a "fit," and after recovery from it he was unable to articulate; there was ptosis with complete ophthalmoplegia of the left eye, with paralysis of the right internal rectus muscle. The following day the right side of the face was found to be completely paralysed. At the autopsy the cerebral vessels were seen to be thickened and atheromatous; the heart was dilated and hypertrophied; the aortic cusps were shortened and

thickened. The innominate artery, the subclavian, and the internal carotid of the same side were completely blocked by thrombus. *See Insp.* 1898, No. 424.

2730 Thrombosis of the Basilar Artery.

A Pons Varolii and medulla mounted to show ante-mortem thrombosis of the main vessels on the ventral surface. The terminal ends of the vertebral and the basilar arteries are filled with firm adherent blood-clot. The vessels are seen to be distinctly thickened and opaque.

Robert Jas. D., æt. 30, was admitted under Dr. Taylor for loss of power in the legs, following upon a "fit" two days previously. He became semi-comatose, and died in a few hours. He had been an in-patient in 1903 for "fits" with headache, unequal pupils, and facial paralysis, and was readmitted in January, 1904, for headache and weakness of the right arm and leg, with left facial paralysis, ptosis, and total left ophthalmoplegia. At the autopsy the cerebral vessels were found to be considerably thickened. The other vessels of the body were healthy. There were two small scars on the liver-capsule. *See Insp.* 1904, No. 163.

DISEASES OF THE VEINS.

2744 Thrombosis of Internal Jugular Vein. Ligature.

A larynx and upper portion of a trachea with the adjacent vessels from the left side of the neck. On the lateral aspect of the specimen the internal jugular vein is seen constricted at the point of application of a ligature, and above this point filled with softening thrombus. Where the vessel is thrombosed the wall is considerably thickened by inflammation.

Maud M., æt. 7, was admitted under Dr. Hale White for a left otorrhœa of four months' duration, associated with signs indicative of disease of the mastoid cells. The mastoid process was trephined, and the internal jugular vein was ligatured and later the lateral sinus. At the autopsy, firm blood-clot was found in the upper part of the lateral sinus extending into the inferior petrosal and circular sinuses, and below the internal jugular vein was occupied by decomposing clot as far as the point of application of the ligature. *See Insp.* 1890, No. 469.

2753 Aneurysm of the External Jugular Vein.

A thin-walled sac which has been divided to show its interior completely filled with blood-clot. In the recent state it measured three and a half inches in its longest diameter and two inches from side to side. The communication between the sac and the external jugular vein is marked by a blue rod.

Charles F., æt. 27, was admitted under Mr. Golding-Bird for a swelling in the neck, which had been noticed since he was twelve years old. Patient stated that he could inflate it by a forced expiration with the mouth shut, while it could be made to disappear on rubbing it with the hand. Twelve days before admission he had been unable to empty it as usual. The swelling was about the size of a closed fist, and was situated behind the angle of the jaw on the right side. The tumour was excised, and the patient was discharged from the hospital two and a half weeks after the date of the operation. *See Surg. Rep.* 1889, vol. 143, No. 42.

2754 Aneurysm of Ulnar Vein.

A small portion of an ulnar vein laid open. A small oval opening leads into a thin-walled sac, which measures about an inch in its longest diameter, and in the recent state was filled with blood.

2755 Aneurysm of the Internal Saphena Vein.

A portion of skin removed from the thigh presenting a smooth, almost spherical projection the size of a cherry, over which the integument is tightly stretched and is so thin as to allow the colour of the subjacent venous tumour to be seen through it. On the reverse of the specimen the vein from which the aneurysm arises has been dissected to show its sinuous course. The vessel is distended with blood-clot.

Harriet B., æt. 45, was admitted under Mr. Golding-Bird for varicose veins on the inner side of the thigh. The venous aneurysm, which was situated just above the head of the tibia on its inner aspect, was excised, and the patient was discharged from the hospital three weeks after the operation. *See Surg. Rep.* 1897, vol. 191, No. 37.

2757 Varicose Vein.

A much dilated and convoluted portion of the internal saphena vein, which together with many smaller varices was removed from the right thigh. The walls of the vein are much thickened, and the vessel is filled with firm blood-clot.

George B., æt. 50, was admitted under Mr. Jacobson with numerous varicose veins on the legs, which had existed for some fifteen years, the right leg being most extensively affected. About eighteen months before admission one of the superficial veins of the right side was noticed to be more swollen than previously, and recently the patient had had considerable pain in the leg on walking. He was discharged from the hospital in a much improved condition three weeks after the varices had been removed. *See Surg. Rep.* 1895, vol. 180, No. 22.

2767 Gummatous Contraction of the Superior Vena Cava.

A portion of a heart with the structures of the mediastinum mounted to show the superior vena cava surrounded by a mass of dense gummatous material and its lumen greatly narrowed. On the reverse of the specimen the right bronchus is seen to be similarly affected.

William H., æt. 59, was admitted under Dr. Goodhart for cyanosis, and œdema of the feet. The heart was enlarged and irregular in its action, and there were signs of aortic incompetence and mitral obstruction. The chest was aspirated on several occasions. The patient became delirious shortly before death, which occurred two months after admission. At the autopsy the heart was found to weigh twenty-six ounces; the aortic and mitral valves were thickened, and the triscupid orifice was dilated. The mediastinal glands were enlarged. *See Insp.* 1889, No. 388.

LIST
OF
GENTLEMEN EDUCATED AT GUY'S HOSPITAL
WHO HAVE PASSED THE
EXAMINATIONS OF THE SEVERAL UNIVERSITIES, COLLEGES,
&c., &c.,
IN THE YEAR 1906.

University of London.

Examination for the Degree of Doctor of Medicine.

Branch I.—*Medicine.*

J. H. Clatworthy.	W. N. May.	G. W. Russell.
J. Evans.	E. B. H. Milsom.	H. F. Bell Walker.
H. C. C. Mann.	E. C. Myott.	B. H. Wedd.
	J. Owen.	

Branch III.—*Mental Diseases and Psychology.*

G. Warwick Smith	S. J. Ormond.
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Branch IV.—*Midwifery and Diseases of Women.*

L. B. Glanville.	A. B. O'Brien.	H. V. Smart.
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Branch V.—*State Medicine.*

M. J. Rees.

Examination for the Degree of Bachelor of Surgery.

Obtained Honours.

R. A. Greeves.

Pass.

G. W. Russell.

Examination for the M.B., B.S. Degrees.

May.

Obtained Honours.

G. Cockcroft (a, d, Gold Medal)	T. B. Layton (d).
H. V. Vandermin (a).	

(a) *Distinguished in Medicine.*

(d) *Distinguished in Surgery.*

Pass.		
A. Alcock.	R. J. Bentley.	T. C. Pocock.
F. Alcock.	P. C. P. Ingram.	T. Turner.

Supplementary Pass List.

Group I.—*Medicine, Pathology, and Forensic Medicine.*

T. P. Hughes.

Examination for the M.B., B.S. Degrees.

October.

Obtained Honours.

W. H. Trethowan (a, d, e, Bracketed for Gold Medal).	A. Pearson, (a). G. F. Stebbing (d).
E. Wragg (b).	

(a) *Distinguished in Medicine.*

(b) *Distinguished in Pathology.*

(d) *Distinguished in Surgery.*

(e) *Distinguished in Midwifery and Diseases of Women.*

Pass.		
T. H. Barton.	I. R. Cook.	P. F. McEvedy.
A. W. Berry.	S. W. Daw.	C. A. L. Mayer.
J. S. Bookless.	E. W. Giesen.	E. F. Reeve.
A. Zorab.		

Supplementary Pass List.

Group I.—*Medicine, Pathology, and Forensic Medicine.*

G. F. E. Allison.

Group II.—*Surgery, Midwifery, and Diseases of Women.*

E. Alban.

Intermediate Examination in Medicine.

January.

M. E. Ball.	†* H. I. Janmahomed.	H. E. H. Mitchell.
*† H. O. Brookhouse.	A. N. Leeming.	P. S. Price.
L. Croft.	A. E. Lees.	D. Reynolds.
T. Evans.	H. C. Lucey.	T. Stansfield.
F. W. Hogarth.	C. H. Marshall.	H. Stott.
K. H. Hole.	J. B. Martin.	

July.

M. M. Cowasjee.	H. B. Kent.	C. C. Tudge.
S. J. Darke.	W. S. Kidd.	C. A. Wood.
A. A. Greenwood.	† R. A. Rankine.	

* *Distinguished in Anatomy.*

† *Distinguished in Physiology.*

*† *Distinguished in Pharmacology.*

Preliminary Scientific Examination.

January.

Part II.—*Organic Chemistry.*

J. L. Atkinson.	C. H. Crump.	D. A. Mitchell.
G. B. Cockrem.	F. W. Hogarth.	T. T. O'Callaghan.
C. Witts.		

Part I.—*Inorganic Chemistry, Experimental Physics, and Biology.*

*P. J. Monaghan.		*P. Smith.		*D. H. Wood.
*D. H. M. Silvanus.		*G. G. Thomson.		

Inorganic Chemistry and Biology.

*J. A. Edmond.		*J. L. Stewart.
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Inorganic Chemistry only.

*W. E. Fox.		*G. T. Mullally.		*R. Stout.
		†B. T. Verver.		

Experimental Physics only.

†E. A. Barker.

Biology only.

L. B. Stringer.		C. Wilson.
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* Denotes completion of Examination.

† Already passed in Biology.

July.

Part II.—*Organic Chemistry.*

R. P. Ballard.	M. A. E. Duvivier.		G. T. Mullally.
W. H. Catto.	H. Gardiner.		E. A. Penny.
F. A. Dick.	G. R. Hind.		R. Stout.
G. Dunderdale.	G. Maxted.		T. D. M. Stout.
	G. Y. Thomson.		

Part I.—*Inorganic Chemistry, Experimental Physics, and Biology.*

G. A. Blake.		L. H. Hopkins.		H. P. Warner.
A. H. Gool.		C. D. Killpack.		

Inorganic Chemistry and Biology.

(p) J. A. Delmege.		(p) A. G. H. Moore.
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Experimental Physics and Biology.

(c) H. Davies.		V. Glendining.
----------------	--	----------------

Inorganic Chemistry only.

(p, b) W. H. T. Jones		(b) S. Wilson.
-----------------------	--	----------------

Experimental Physics only.

G. Covell.		(b) L. B. Stringer.
------------	--	---------------------

Biology only.

C. Aldis.		E. G. Reeve.		(c, p) A. H. Todd.
F. C. Hunôt.		T. E. Roberts.		

(b) Has already passed in Biology.

(c) Has already passed in Inorganic Chemistry.

(p) Has already passed in Experimental Physics.

Intermediate Examination in Science.

F. Cook.		E. G. Schlesinger.		A. H. Todd.
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University of Oxford.

Degree of Doctor of Medicine.

W. L. M. Day.

|

W. E. Robinson.

Second M.B. Examination.

Medicine, Surgery, Midwifery, Forensic Medicine and Public Health.

R. Evans.

Pathology.

C. G. Douglas.

University of Cambridge.

Degree of Master in Surgery (M.Ch.).

E. C. Hughes.

|

W. M. Mollison.

Third Examination for the Medical and Surgical Degrees.

Part II.

A. S. B. Bankart.
F. A. Barker.
H. J. Clarke.
R. Davies-Colley.

C. F. Fothergill.
G. W. Goodhart.
P. P. Laidlaw.
B. K. Nutman.

A. S. Morton Palmer.
C. H. Rippmann.
W. H. Robinson.
A. Walker.

Part I.

F. A. Barker.
H. B. Carlyll.

E. B. Hinde.
B. K. Nutman.
R. R. Walker.

B. H. Palmer.
C. H. Rippmann.

Second Examination for the Medical and Surgical Degrees.

H. L. Attwater.
L. Bromley.
H. L. Duke.

W. Ledlie.
H. Lee.
H. F. Percival.

C. F. Searle.
V. T. P. Webster.

University of Durham.

April.

*Examination for the Degree of Doctor in Medicine for Practitioners
of Fifteen Years' Standing.*

H. Joslen.

Third Examination for the Degree of Bachelor in Medicine.

J. F. Young.

Second Examination for the Degree of Bachelor in Medicine.

L. W. Evans. | A. C. Greene. | S. L. Randolph.

First Examination for the Degree of Bachelor in Medicine.

W. Reynolds.

Elementary Anatomy and Biology.

G. E. W. Lacey.

Chemistry and Physics.

E. W. Blake.

Royal College of Physicians of London.

Elected to the Fellowship.

M. Craig.

Final Examination for the License.

January.

A. H. Clough.	T. B. Layton.	W. P. Purdom.
C. C. A. De Villiers.	L. Myer.	S. Reader.
C. W. Gibson.	N. H. Oliver.	A. Walker.
T. W. Kirby.	W. S. Orton.	H. D. Wyatt.

April.

A. S. B. Bankart.	C. W. Greene.	A. M. Roome.
G. N. Bartlett.	R. A. Greeves.	T. Turner.
R. Davies-Colley.	R. S. Harper.	H. F. Vandermin.
C. F. Fothergill.	J. O. Musson.	G. Wachter.

July.

R. D. Barron.	P. F. McEvedy.	G. W. Ponder.
W. H. S. Burney.	H. C. Malleson.	Richard P. Rowlands.
S. W. Daw.	W. H. Miller.	G. F. Stebbing.
E. W. Giesen.	C. M. Ockwell.	P. R. Taraporwala.
P. C. Litchfield.	H. A. Pallant.	E. Wragg.

October.

E. H. Adams.	P. D. F. Magowan.	R. M. Rendall.
E. Alban.	C. A. L. Mayer.	A. T. Rivers.
A. W. Berry.	H. V. Mitchell.	H. E. H. Tracey.
I. R. Cook.	E. Morgan.	W. H. Trethowan.
L. Doudney.	T. Norman.	I. Valerio.
J. S. Farnfield.	G. R. Phillips.	A. Zorab.

Royal College of Physicians of Edinburgh.

Examination for the Membership.

A. Kinsey-Morgan.

Royal College of Surgeons of England.

Final Examination for the Fellowship.

P. P. Cole.	E. C. Hughes.	G. C. F. Robinson.
R. A. Greeves.	W. M. Mollison.	A. M. Webber.

First Examination for the Fellowship.

H. Chapple.	A. N. Leeming.	H. Joste Smith.
J. S. Cooper.	C. F. L. Leipoldt.	V. Townrow.
H. I. Janmahomed.	C. M. Plumptre.	

Final Examination for the Membership.

January.

A. H. Clough.	T. B. Layton.	W. P. Purdom.
C. C. A. De Villiers.	L. Myer.	S. Reader.
C. W. Gibson.	N. H. Oliver.	A. Walker.
T. W. Kirby.	W. S. Orton.	H. D. Wyatt.

April.

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R. Davies-Colley.	R. S. Harper.	H. F. Vandermin.
C. F. Fothergill.	J. O. Musson.	G. Wachter.

July.

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W. H. S. Burney.	H. C. Malleson.	Richard P. Rowlands.
S. W. Daw.	W. H. Miller.	G. F. Stebbing.
E. W. Giesen.	C. M. Ockwell.	P. R. Taraporwala.
P. C. Litchfield.	H. A. Pallant.	E. Wragg.

October.

E. H. Adams.	P. D. F. Magowan.	B. M. Rendall.
E. Alban.	C. A. L. Mayer.	A. T. Rivers.
A. W. Berry.	H. V. Mitchell.	H. E. H. Tracey.
I. R. Cook.	E. Morgan.	W. H. Trethowan.
L. Doudney.	T. Norman.	I. Valerio.
J. S. Farnfield.	G. R. Phillips.	A. Zorab.

**Conjoint Examining Board in England—Diploma in
Public Health.**

G. E. Malcomson.		J. F. Northcott.
Lieutenant-Colonel T. B. Winter, R.A.M.C.		

Royal Navy Medical Department.

F. G. Goble.		P. F. Minett.
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Royal Army Medical Corps.

A. M. Benett.		C. H. Denyer.
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Indian Medical Service.

G. E. Malcomson.		P. S. Mills.
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MEDALLISTS AND PRIZEMEN,

JULY, 1906.

Open Scholarships in Arts.

Herbert Leslie Hopkins, Owen's School, Islington, £100.

Alan Herapath Todd, Sherborne School, £50.

Open Scholarships in Science.

Maro Antoine Emile Duvivier, Guy's Hospital Medical School, £150.

Thomas Duncan MacGregor Stout,	} equal,	£30 each.
Guy's Hospital Medical School		
Arthur Neville Cox, Derby School		

Scholarship for University Students.

Claude Gordon Douglas, B.A., Magdalen College, Oxford, £50.

Harold Chapple, B.A., St. John's College, Cambridge, Certificate.

Open Scholarships in Dental Mechanics.

October, 1905.

Ernest James Archer	} equal, £10 each.
William Edwin Guilding	

May, 1906.

Dudley Bayzand Tasker, £20.

Junior Proficiency Prizes.

Hugh Braund Kent, £20.

Charles Albert Wood, £15.

Sidney John Darke, £10.

Arthur Atkins Greenwood, Certificate.

The Michael Harris Prize for Anatomy.

Hugh Braund Kent, £10.

The Wooldridge Memorial Prize for Physiology.

John Lee Atkinson, £10.

Hugh Braund Kent, Certificate.

The Hilton Prize for Dissections.

Hugh Braund Kent	}	equal, £2 10s. each.
William Edgar Williams		

The Arthur Durham Prizes for Dissection.

First Year's Students.

Richard Pitt Ballard, £5.

Senior Students.

Hugh Braund Kent, £15.

William Edgar Williams, Certificate.

Arthur Atkins Greenwood, Certificate.

Dental Prizes.

First Year's Students.

Hedley Clarence Visick, £50

Treasurer's Gold Medal for Clinical Medicine.

Patrick Playfair Laidlaw.

Treasurer's Gold Medal for Clinical Surgery.

George Cockcroft.

THE PHYSICAL SOCIETY.

Honorary President.—Sir Samuel Wilks, Bart., M.D., LL.D., F.R.S.

Honorary Vice-Presidents.—J. F. Goodhart, M.D., LL.D., Sir Henry Howse, M.S., P. H. Pye-Smith, M.D., F.R.S., G. H. Savage, M.D.

Presidents.—K. H. Digby, M.B., B.S., C. W. Greene, B.A., M.B., B.C., C. F. L. Leipoldt, T. B. Layton, M.B., B.S., G. W. Goodhart, M.A., M.B., B.C., P. P. Laidlaw, M.A., B.C., C. H. Rippmann, M.A., B.C., E. P. Minett, G. F. Stebbing, M.B., B.S., W. H. Trethowan, M.B., B.S., J. N. Watson, N. Flower, B.A., J. Lee Atkinson, H. Joste Smith, M.B., B.S.

Hon. Secretaries.—W. M. Mollison, M.A., M.C., G. W. Nicholson, M.A., M.D.

Session 1906-1907.—The Society's prize of £10 for the best essay read during the Session was given to Mr. T. B. Layton for his paper, "The Anatomy of the Growth of the Long Bones in its Relation to Injury and Disease."

The Treasurer's prize of £5 was awarded to Mr. C. H. Rippmann for his essay on Pneumococcal Suppuration.

The prize for the best specimens exhibited was divided: Mr. W. P. Purdom received £3, Mr. E. P. Minett and Mr. R. P. M. Roberts £1 each.

CLINICAL APPOINTMENTS HELD DURING THE YEAR 1906.

HOUSE PHYSICIANS.

O. V. Payne
A. B. O'Brien
H. S. Knight
E. B. Smith

R. O. Williams
H. C. Cameron
G. Hamilton

R. A. Chisolm
R. E. French
G. H. K. MacAlister

HOUSE SURGEONS.

H. M. Clarke
S. M. Wells
W. Reeve
E. M. Harrison

W. N. May
A. G. Jones
A. V. Maybury

A. Leeming
C. M. Stevenson
L. G. Davies

ASSISTANT HOUSE SURGEONS.

R. Edridge
V. A. P. Costobadie
E. C. Lowe
G. W. Nicholson
A. S. Bankart
P. S. Mills

H. A. Watney
A. H. Miller
E. B. Smith
H. F. Vandermin
A. S. M. Palmer

W. Reeve
E. M. Harrison
G. N. Bartlett
W. P. Purdom
W. Welchman

OUT-PATIENTS' OFFICERS.

H. C. Cameron
C. M. Stevenson
W. Reeve
E. M. Harrison
A. Alcock
W. P. Purdom

R. E. French
G. Hamilton
A. V. Maybury
G. H. K. MacAlister
R. Davies-Colley

A. G. Jones
H. S. Knight
L. G. Davies
E. B. Smith
T. B. Layton

OBSTETRIC RESIDENTS.

A. M. Webber	G. A. Ticehurst	F. Alcock
A. D. Crofts	V. A. P. Costobadie	H. D. Wyatt
E. C. Lowe	H. A. Watney	R. E. French
G. Wachter		

CLINICAL ASSISTANTS.

G. Hamilton	E. M. Harrison	H. S. Knight
E. C. Lowe	A. V. Maybury	E. B. Smith
H. A. Watney	G. Cockcroft	L. G. Davies
G. H. K. MacAlister	G. W. Nicholson	W. P. Purdom
W. Welchman	A. Alcock	A. S. B. Bankart
R. Davies-Colley	T. B. Layton	A. S. M. Palmer
G. N. Bartlett	W. H. S. Burney	H. C. Malleison
W. H. Miller	R. P. Rowlands	H. F. Vandermin

CLINICAL ASSISTANTS IN THE MEDICAL WARDS.

E. P. Joynt	M. M. Earle	C. A. Basker
E. P. Minett	L. Croft	P. P. Laidlaw
F. A. Barker	B. K. Nutman	C. W. Ponder
H. V. Mitchell	R. Evans	W. H. Miller
W. R. Greening	A. S. B. Bankart	J. H. Mayston
C. W. Greene		

CLINICAL ASSISTANTS IN THE SURGICAL WARDS.

A. S. M. Palmer	H. E. H. Tracy	C. F. Fothergill
L. J. J. Orpen	R. S. Harper	B. B. Metcalfe
T. E. A. Carr	C. F. L. Leipoldt	R. Evans
J. S. Farnfield	A. W. Eyles	A. T. Rivers
F. Morris	J. H. Mayston	C. H. Marshall
J. L. Rankine		

SURGEONS' DRESSERS.

H. F. Joynt	R. G. Chase	R. Evans
R. B. Dawson	C. H. Marshall	J. W. Featherstone
G. W. Dryland	H. J. B. Cane	L. D. Stamp
P. K. Taraporwalla	H. J. Henderson	A. L. Foster
C. B. Ticehurst	N. Flower	H. B. Carlyll
C. H. Rippmann	E. B. Hinde	G. G. Timpson
H. J. Smith	A. T. Densham	T. N. Wood
R. R. Walker	J. M. Watson	A. V. Ledger
J. W. Grice	F. Morris	E. A. Collins
T. H. Edey	M. R. Dobson	S. H. C. Air
B. H. Palmer	K. H. Digby	H. P. Aubrey
E. P. Minett	W. W. Cook	M. D. Price
J. B. Martin	L. Croft	R. B. Dawson
J. B. Ball	C. D. Roberts	M. J. Rattray
L. L. C. Reynolds.	J. H. Ryffel	C. E. Price
M. A. Rahman	W. G. Pinching	F. H. Fuller
J. B. Martin	M. K. Nelson	P. J. Kolaporewalla
A. F. W. Denning	H. E. Perkins	L. T. Baker
J. F. Young	R. C. Edsall	T. Evans
A. W. Ewing	R. P. M. Roberts	L. K. Edmeades
A. H. St. John	A. C. Dickson	C. H. Mills
H. Stott	M. E. Ball	H. E. Perkins
F. W. Hogarth	C. G. Douglas	L. T. Dean

OPHTHALMIC DRESSERS.

B. B. Metcalfe	A. Zorab	J. S. Bookless
R. S. Harper	G. W. Goodhart	T. B. Layton
R. Willan	F. A. Barker	M. M. Earle
C. E. M. Jones	J. L. Rankine	C. M. Ockwell
E. L. R. Norton	H. C. Malleeson	E. Morgan
E. P. Minett	J. W. Featherstone	W. W. Cook
C. W. Greene	B. Wallis	M. J. Rattray
J. E. Prentis	T. E. A. Carr	G. F. E. Allison
C. A. L. Mayer	C. B. Ticehurst	

CLINICAL ASSISTANTS IN MEDICAL OUT-PATIENTS.

R. J. Bentley	S. K. Poole	M. M. Earle
T. R. Harvey	C. A. L. Mayer	E. B. Hinde

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C. M. Ockwell	W. P. Purdom	W. H. Trethowan
F. B. Lowe	A. W. Eyles	T. B. Layton
J. S. Farnfield	T. Turner	G. Wachar
J. S. Bookless	A. Zorab	S. W. Daw
E. Wragg	G. W. Dryland	C. B. Ticehurst
G. W. Goodhart	J. H. Mayston	E. Morgan
W. P. H. Munden	J. L. Rankine	G. F. Stebbing.

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L. Croft	S. H. C. Air	W. W. Cook
M. D. Price	J. B. Martin	E. P. Minett
M. R. Dobson	C. D. Roberts	B. H. Palmer
L. T. Dean	C. H. Mills	E. A. Collins
P. V. G. Pedrick	F. W. Hogarth	J. F. Young
T. Evans	D. Reynolds	R. G. Chase
M. E. Ball	H. Stott	A. W. Ewing
C. G. Douglas	L. T. Baker	F. W. Denning
R. P. M. Roberts	L. K. Edmeades	C. E. Price
H. E. Perkins	A. C. Dickson	G. F. Symms
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J. H. Ryffel	J. Walker	P. J. Kolaporewalla
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K. H. Hole	J. B. Dunning	H. O. Brookhouse
L. Mandel	A. E. Lees	H. R. Mullins
H. E. H. Mitchell	S. S. Brook	H. I. Shahn
H. Chapple	V. P. Hutchinson	C. A. Wood
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B. McDermott	J. Walker	H. I. Jannmahomed
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V. Townrow	C. F. Searle	A. E. Rayner
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J. F. Young	R. G. Chase	A. W. Ewing
L. K. Edmeades	M. E. Ball	C. G. Douglas
L. T. Dean	F. W. Hogarth	A. N. Leeming
H. C. Lucey	R. C. V. Edsall	R. P. M. Roberts
C. H. Mills	E. P. L. Hughes	J. B. Dunning
J. Walker	F. J. Wheeler	H. B. Carter
C. S. E. Wright	E. L. M. Lobb	G. F. Syms
W. Johnson	E. R. Stone	F. J. Cutler
D. Reynolds	H. R. Mullins	H. Chapple
H. O. Brookhouse	S. S. Brook	A. E. Lees
H. E. H. Mitchell	K. H. Hole	H. I. Shahin
L. Mandel	V. P. Hutchinson	H. A. Sanford
P. S. Price	D. Allan	

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S. L. Randolph	M. M. Adams	H. I. Janmahomed

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T. Turner	T. Norman	C. C. De Villiers
L. D. Stamp	J. E. Hodson	R. R. Walker
H. B. Carlyll	H. F. Joynt	

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A. W. Eyles	C. A. L. Mayer	E. P. H. Joynt
H. F. Joynt		

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C. M. Ockwell
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J. E. Hodson
E. L. R. Nerton

L. J. J. Orpen
R. Davies-Colley
G. W. Goodhart
M. J. Rattray

R. J. Bentley
W. H. S. Burney
C. W. Greene

POST-MORTEM CLERKS.

A. N. Leeming
G. Douglas
C. A. Basker
B. K. Nutman
St. J. A. M. Tolhurst
E. Wragg
A. Pearson
M. E. Ball
L. Croft
E. P. H. Joynt
J. W. Grice
J. B. Dunning
F. Morris

M. D. Price
A. Zorab
W. P. H. Munden
G. F. Allison
S. W. Daw
H. J. Smith
A. W. Eyles
L. T. Baker
H. J. Henderson
C. F. L. Leipoldt
M. R. Dobson
H. J. B. Cane

C. E. M. Jones
J. F. Young
R. J. Reynolds
D. Reynolds
E. W. Giesen
R. R. Walker
C. A. L. Mayer
L. K. Edmeades
K. H. Digby
C. H. Rippmann
C. H. Marshall
H. F. Joynt.

OBSTETRIC DRESSERS.

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T. B. Layton
G. N. Bartlett
E. Wragg
P. F. McEvedy
C. A. L. Mayer
G. F. Stebbing
S. McK. Saunders
H. F. Joynt
R. Evans
J. T. Smalley

J. G. Phillips
G. F. E. Allison
W. H. Miller
A. Alcock
A. Zorab
J. E. Hodson
W. P. H. Munden
C. F. L. Leipoldt
St. J. A. M. Tolhurst
R. J. Reynolds
H. F. Hardy

J. L. Rankine
E. Alban
S. W. Daw
E. W. Giesen
C. W. Greene
T. E. A. Carr
C. A. Basker
S. K. Poole
E. P. Minett
H. J. Smith

CLERKS TO ANÆSTHETISTS.

G. R. Phillips
A. T. Rivers
W. H. Miller
F. A. Barker
T. R. Harvey
H. J. B. Cane
G. G. Timpson
A. L. Foster
K. H. Digby
S. H. C. Air
B. K. Nutman
M. J. Rattray
B. Wallis
R. Evans
E. T. Tuck
J. N. Watson
E. B. Hinde
A. N. Leeming
C. H. Rippmann
P. P. Laidlaw
M. K. Nelson
N. Flower
M. R. Dobson
L. Croft
J. B. Martin
M. A. Rahman

P. F. McEvedy
E. W. Giesen
W. P. H. Munden
A. Davidson
C. A. Basker
T. E. A. Carr
G. F. Stebbing
J. H. Mayston
E. P. H. Joynt
C. H. Marshall
C. B. Ticehurst
H. F. Joynt
F. C. Knight
G. W. Dryland
E. Wragg
P. N. May
T. N. Wood
R. G. Chase
F. J. Kolaporewalla
S. K. Poole
B. H. Palmer
H. B. Carlyll
R. P. Rowlands
C. W. Gibson
F. H. Fuller

R. J. Reynolds
L. L. C. Reynolds
S. W. Daw
J. T. Smalley
J. S. Farnfield
St. J. A. M. Tolhurst
P. P. Laidlaw
G. F. A. Allison
C. F. L. Leipoldt
D. Reynolds
R. R. Walker
H. J. Henderson
W. W. Cook
S. McK. Saunders
J. E. Featherstone
T. H. Edey
F. Morris
L. D. Stamp
A. S. Densham
J. W. Grice
J. H. Ryffel
A. V. Ledger
H. P. Aubrey
L. T. Baker
M. E. Ball

DENTAL SCHOOL

CLINICAL APPOINTMENTS HELD DURING THE YEAR 1906.

HOUSE SURGEONS.

J. A. Bowes		S. G. Elliott		J. McBride		H. E. Marsh
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ASSISTANT HOUSE SURGEONS.

T. M. Holborn		H. E. Marsh		J. R. D. Ditch
C. C. Freer		I. Margolies		W. S. Rutter
N. V. H. Riches		H. C. Visick		

DEMONSTRATORS IN THE CONSERVATION ROOM.

J. R. D. Ditch		C. G. G. Lewis		I. Margolies
W. T. Clarke		R. Redpath		W. S. Rutter
H. J. Dear		W. G. Oliver		H. S. Visick
J. W. Doherty		P. E. Kendall		I. S. Spain

ASSISTANT DEMONSTRATORS IN DENTAL MECHANICS.

C. C. Freer		B. L. Weaver		W. L. Power
-------------	--	--------------	--	-------------

ASSISTANT DEMONSTRATORS IN DENTAL MICROSCOPY.

W. F. Boxall		I. Margolies
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ASSISTANT DEMONSTRATORS IN DENTAL METALLURGY.

H. L. Power		N. V. H. Riches.
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DRESSEERS IN THE GAS ROOM.

L. B. Moore		R. Beadnell Gill		J. E. O. Brawn
G. L. Davies		H. G. Dumayne		G. Warren
H. T. Reeve		J. R. D. Ditch		T. L. Smith
R. J. Oliver		H. V. Sharp		E. Barnett
H. J. Dear		I. Margolies		R. A. Glendon
N. P. Rodgers		O. G. Iliffe		G. Packham
A. H. Pickett		H. Simms		W. T. Clarke
A. E. Webb		R. M. Wormald		W. F. Boxall
R. Redpath		E. L. Brown		W. S. Rutter
W. G. Oliver		H. C. Visick		A. H. Gabell
R. R. B. Ponder		W. C. McN. Dickey		J. E. Hanna
V. Masters		A. F. Hochapfel		M. J. Marks
F. Giles		C. R. Rudolf		E. G. Robertson
P. E. Kendall		J. R. Palmer		R. G. Gibbings
H. O. Salt		I. S. Spain		W. F. Whiteley
S. W. Chetwood		J. W. Doherty		G. Hunt
R. M. King		H. G. Clarke		F. N. Doubleday
R. P. Fenn				

DRESSERS IN THE EXTRACTION ROOM.

J. W. Doherty	G. Hunt	D. Y. Hylton
R. M. Wormald	H. C. Visick	H. Sturton
S. W. Chetwood	E. G. Robertson	I. S. Spain
P. E. Kendall	G. H. Hickman	A. F. Hochapfel
F. N. Doubleday	R. M. King	J. B. Boxall
P. J. Proud	H. P. Tait	W. A. Dredge
W. J. Kennealy	P. R. Helyar	W. F. Whiteley
A. L. Saul	M. J. Marks	H. Walker
R. J. Gibbings	L. J. Kemp	F. O. Hume
A. Samuel	C. R. M. Peaty	E. J. Archer
W. E. Guilding	C. C. Jones	L. A. B. King
F. Townend	I. Levy	A. M. Henry
R. M. King	E. W. Sumpter	A. Cohen
H. V. Gibbons	E. E. Solomon	D. B. Tasker
R. C. Morgan	W. A. James	P. Harrison
E. Smith	W. E. Watson	

CASUALTY DRESSERS.

E. Barnett	H. J. Dear	F. Giles
W. G. Oliver	W. F. Boxall	A. H. Gabell
H. C. Visick	H. Sturton	R. M. Wormald
A. F. Hochapfel	P. E. Kendall	J. R. Palmer
J. W. Doherty	E. G. Robertson	H. O. Salt
I. S. Spain	W. C. McN. Dickey	D. Y. Hylton
R. M. King	M. J. Marks	B. J. Gibbings
C. R. M. Peaty	A. Samuel	I. Levy
G. Hunt	F. N. Doubleday	P. R. Helyar
H. Walker	S. W. Chetwood	P. J. Proud
H. P. Tait	W. F. Whiteley	W. A. Dredge
F. O. Hume	A. M. Henry	E. J. Archer
C. C. Jones	L. A. B. King	D. B. Tasker

DRESSERS IN THE CONSERVATION ROOM.

H. G. Clark	H. Walker	R. P. Fenn
W. E. Freeman	S. G. Elliott	C. G. G. Lewis
C. Lloyd	R. A. Glindon	H. L. Power
H. T. Reeve	E. S. Pierrepont	H. V. Sharp
G. Warren	B. B. Samuel	E. L. Brown
J. E. Hanna	C. C. Freer	N. V. H. Riches
N. P. Rodgers	A. H. Pickett	W. J. P. Dicks
F. Giles	C. R. Rudolf	L. B. Moore
W. J. C. Timberlake	J. S. Vogweil	J. E. O. Brawn
W. T. Clarke	A. S. Thomas	J. R. D. Ditch
W. Elwood	G. L. Davies	H. Simms
W. S. Rutter	W. F. Boxall	H. G. Dumayne
V. Masters	R. J. Oliver	H. Sturton
H. C. Visick	R. M. Wormald	D. Y. Hylton
H. J. Dear	A. H. Gabell	I. Margolies
F. J. Gillett	W. G. Oliver	R. R. B. Ponder
A. E. Webb	R. Beadnell Gill	L. A. B. King
R. Redpath	W. J. Kennealy	G. Packham
R. J. Gibbings	M. J. Marks	W. S. Rutter
T. Townend	H. Hunt	W. J. Doherty
W. E. Guilding	I. S. Spain	P. J. Proud
H. O. Salt	O. Roots	H. P. Tait
F. A. Beckley	J. R. Palmer	E. G. Robertson
O. G. Illiffe	P. E. Kendall	L. B. Moore

PROBATIONARY DRESSERS.

S. W. Chetwood
A. F. Hochapfel
R. M. King
P. J. Proud
A. L. Saul
W. F. Whiteley
F. N. Doubleday
A. M. Henry
C. C. Jones
L. A. B. King
I. S. Spain
W. A. Dredge
L. J. Kemp
H. Daw
R. C. Morgan
D. B. Tasker

W. A. Dredge
F. O. Hume
M. J. Marks
E. G. Robertson
H. P. Tait
A. J. Archer
W. E. Guilding
G. H. Hickman
P. E. Kendall
I. Levy
T. Townend
A. M. Henry
H. V. Gibbons
E. E. Solomon
A. Cohen

R. J. Gibbings
C. M. Peaty
A. Samuel
H. Walker
J. W. Doherty
P. R. Helyar
G. Hunt
W. J. Kennealy
J. R. Palmer
A. J. Partridge
S. W. Chetwood
F. O. Hume
P. Harrison
E. Smith
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GUY'S HOSPITAL.

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1907.

Consulting Physicians.—SIR SAMUEL WILKS, BART., M.D., LL.D., F.R.S.; F. W. PAVY, M.D., LL.D., F.R.S.; P. H. PYE-SMITH, M.D., F.R.S.; J. F. GOODHART, M.D., LL.D.; F. TAYLOR, M.D.

Consulting Surgeons.—THOMAS BRYANT, M.Ch.; Sir H. G. HOWSE, M.S.; W. H. A. JACOBSON, M.Ch.; R. CLEMENT LUCAS, B.S.

Consulting Obstetric Physician.—A. L. GALABIN, M.D.

Consulting Physician for Mental Diseases.—G. H. SAVAGE, M.D.

Consulting Ophthalmic Surgeons.—C. HIGGINS, Esq.; W. A. BRAILEY, M.D.

Consulting Aural Surgeon.—W. LAIDLAW PURVES, M.D.

Consulting Dental Surgeon.—F. NEWLAND-PEDLEY, Esq.

Consulting Anæsthetist.—TOM BIRD, Esq.

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J. H. TARGETT, M.S.

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G. BELLINGHAM SMITH, M.B., B.S.

Surgeon in Charge of Throat Department.

F. J. STEWARD, M.S.

Physician for Mental Diseases.

MAURICE CRAIG, M.D.

Surgeon in Charge of Aural Department.

C. H. FAGGE, M.S.

Physician in Charge of Skin Department.

SIR E. COOPER PERRY, M.D.

Surgeon in Charge of Actino-Therapeutic Department.

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R. WYNNE ROUW, Esq.

H. L. PILLIN, Esq.

M. F. HOPSON, Esq.

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J. B. PARFITT, Esq.

J. L. PAYNE, Esq.

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A. S. B. BANKART, Esq.

Obstetric Registrar and Tutor.

R. DAVIES-COLLEY, B.C.

Ophthalmic Registrars and Clinical Assistants.

W. ANDERSON, M.D.

W. M. BERGIN, M.B.

Resident Surgical Officer.

E. C. HUGHES, M.C.

Curator of the Museum.

J. FAWCETT, M.D.

Warden of the College.

W. M. MOLLISON, M.C.

Lying-in Charity.

Mr. TARGETT and Mr. BELLINGHAM SMITH.

Dean of the Medical School.

H. L. EASON, M.D., M.S.

MEDICAL SCHOOL STAFF.

1907.

Medicine.

<i>Clinical Medicine</i>	THE PHYSICIANS AND ASSISTANT PHYSICIANS.
<i>Principles and Practice of Medicine</i> (Lectures)	THE PHYSICIANS.
<i>Practical Medicine</i>	H. C. C. MANN, M.D., AND H. C. CAMERON, M.B., B.C.
<i>Medical Revision Classes</i>	H. S. FRENCH, M.D.

Surgery.

<i>Clinical Surgery</i>	THE SURGEONS AND ASSISTANT SURGEONS.
<i>Principles and Practice of Surgery</i> (Lectures)	CHARTERS J. SYMONDS, M.S., W. ARBUTHNOT LANE, M.S., AND L. A. DUNN, M.S.
<i>Operative Surgery</i>	C. H. FAGGE, M.S., R. P. ROWLANDS, M.S. Demonstrator, P. TURNER, M.S.
<i>Practical Surgery</i>	G. HAMILTON, M.B., B.S., AND A. S. B. BANKART, ESQ.
<i>Surgical Revision Classes</i>	C. H. FAGGE, M.S.

Obstetrics and Gynaecology.

<i>Clinical Gynaecology</i>	THE OBSTETRIC PHYSICIANS AND ASSISTANT OBSTETRIC PHYSICIAN.
<i>Obstetrics and Gynaecology</i> (Lectures)	P. HORROCKS, M.D., AND J. H. TARGETT, M.S.
<i>Practical Obstetrics</i>	R. DAVIES-COLLEY, B.C.
<i>Obstetric Revision Classes</i>	G. BELLINGHAM SMITH, M.B., B.S.

Pathology.

<i>Pathology</i> (Lectures)	A. E. BOYCOTT, M.D.
<i>Morbid Histology</i>	A. E. BOYCOTT, M.D.
<i>Morbid Anatomy</i> (Demonstrations) in Post-mortem Room	J. FAWCETT, M.D., AND H. S. FRENCH, M.D.
<i>Surgical Pathology</i> (Demonstrations)	R. P. ROWLANDS, M.S.
<i>Medical Pathology</i> (Demonstrations)	J. FAWCETT, M.D.

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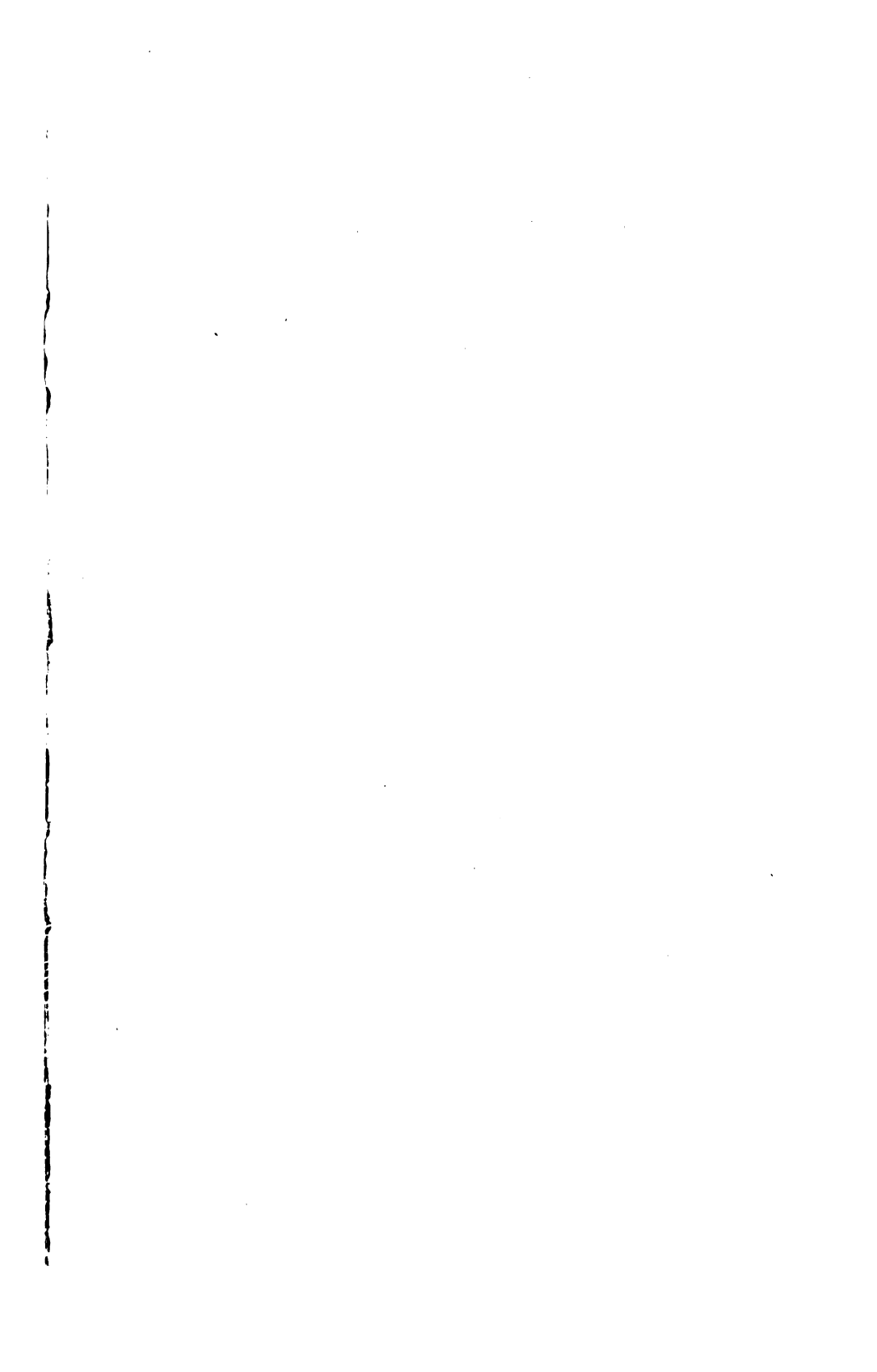
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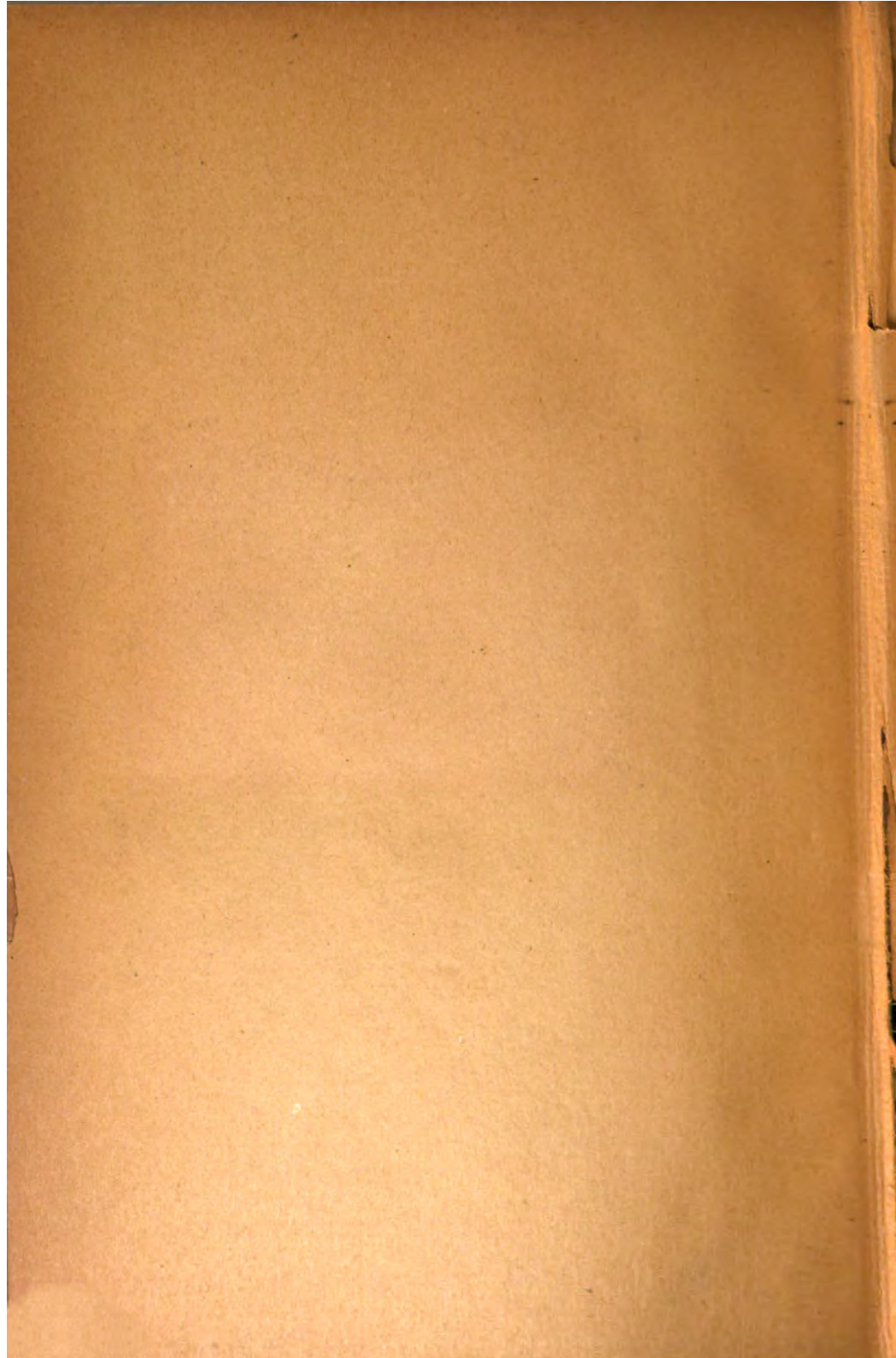
CONTENTS.

1. The Chronic Relapsing Pyrexia of Hodgkin's Disease. By Frederick Taylor, M.D.
 2. Mitral Stenosis and Pregnancy. By Herbert French, M.D., and H. T. Hicks, F.R.C.S.
 3. Life and Mechanism. Two Lectures delivered at the Physiological Laboratory, Guy's Hospital, May 17th and 24th, 1906. By J. S. Haldane, M.D., F.R.S.
 4. Secretion by the Renal Tubules in the Frog. By F. A. Bainbridge, M.A., M.D., and A. P. Beddard, M.A., M.D.
 5. Two Cases of Malignant Embryoma of the Ovary. By J. H. Targett, M.S., F.R.C.S., and H. T. Hicks, F.R.C.S.
 6. A Note upon the Relation of Traumatic Diabetes Insipidus to Glycosuria. By Herbert French, M.D., and C. B. Ticehurst, B.A.
 7. The Fate of the Ovum and Graafian Follicle in Præ-Menstrual Life. By Thos. G. Stevens, M.D.
 8. The Prevalence of Trichocephalus Dispar. By Herbert French, M.D., and A. E. Boycott, M.D.
 9. Carcinoma and Gastric Hydrochloric Acid. Thesis for Degree of M.D. Cambridge. By F. W. Morton Palmer, M.A., M.B., B.C.
 10. Notes on the Examination of the Blood. By A. E. Boycott, M.D.
 11. Vaccines as an Aid to Surgery and Medicine. By Maurice G. Louisson, M.B., B.S.
 12. Pyelonephritis as a Complication of Pregnancy. By G. Bellingham Smith.
 13. The Pathology and Treatment of CEdema, with special reference to the Influence of Diminished Excretion of Sodium Chloride on its Production. By Arthur F. Hertz, M.A., M.B. Oxon., M.R.C.P.
 14. Meckel's Diverticulum and its Pathology. By Philip Turner, M.S., B.Sc., F.R.C.S.
 15. The Platinochloride Test for Choline in Human Blood. By R. W. Allen, M.A., and Herbert French, M.A., M.D.
 16. Some Observations on the Effects Produced by Choline upon Animals. By E. Farquhar Buzzard, M.D., and R. W. Allen.
- List of Gentlemen Educated at Guy's Hospital who have passed the Examinations of the several Universities, or obtained other Distinctions, during the year 1904.
Medallists and Prizemen for 1905.
The Physical Society, 1904.
Clinical Appointments held during the year 1904.
Dental Appointments held during the year 1904.
List of Gentlemen Educated at Guy's Hospital who have passed the Examinations of the several Universities, or obtained other Distinctions, during the year 1905.
The Physical Society, 1905.
Clinical Appointments held during the year 1905.
Dental Appointments held during the year 1905.
Medical and Surgical Staff, 1906.
Medical School Staff—Lecturers and Demonstrators.
The Staff of the Dental School, 1906.

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